UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
WASHINGTON, DC 20549

Form 10-K

(Mark One)

☒ **ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**
For the fiscal year ended December 31, 2025
or
☐ **TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**
For the transition period from _____ to
Commission File Number: 001-38583

Crinetics Pharmaceuticals, Inc.

(Exact name of registrant as specified in its charter)

Delaware	**26-3744114**
(State or other jurisdiction of incorporation or organization)	(I.R.S. Employer Identification No.)

6055 Lusk Boulevard, San Diego, California, 92121
(Address, including zip code, of principal executive offices)

Registrant's telephone number, including area code: **(858) 450-6464**

Securities registered pursuant to Section 12(b) of the Act:

Title of Each Class	Trading Symbol(s)	Name of Each Exchange on Which Registered
Common Stock, par value $0.001 per share	**CRNX**	**Nasdaq Global Select Market**

Securities registered pursuant to Section 12(g) of the Act: None

Indicate by check mark if the registrant is a well-known seasoned issuer, as defined in Rule 405 of the Securities Act. Yes ☒ No ☐

Indicate by check mark if the registrant is not required to file reports pursuant to Section 13 or 15(d) of the Act. Yes ☐ No ☒

Indicate by check mark whether the registrant: (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the registrant was required to file such reports), and (2) has been subject to such filing requirements for the past 90 days. Yes ☒ No ☐

Indicate by check mark whether the registrant has submitted electronically every Interactive Data File required to be submitted pursuant to Rule 405 of Regulation S-T (§232.405 of this chapter) during the preceding 12 months (or for such shorter period that the registrant was required to submit such files). Yes ☒ No ☐

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, a smaller reporting company or an emerging growth company. See definitions of "large accelerated filer," "accelerated filer," "smaller reporting company" and "emerging growth company" in Rule 12b-2 of the Securities Exchange Act of 1934.

Large accelerated filer	☒	Accelerated filer	☐	Emerging growth company	☐
Non-accelerated filer	☐	Smaller reporting company	☐		

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☐

Indicate by check mark whether the registrant has filed a report on and attestation to its management's assessment of the effectiveness of its internal control over financial reporting under Section 404(b) of the Sarbanes-Oxley Act (15 U.S.C. 7262(b)) by the registered public accounting firm that prepared or issued its audit report. ☒

If securities are registered pursuant to Section 12(b) of the Act, indicate by check mark whether the financial statements of the registrant included in the filing reflect the correction of an error to previously issued financial statements. ☐

Indicate by check mark whether any of those error corrections are restatements that required a recovery analysis of incentive-based compensation received by any of the registrant's executive officers during the relevant recovery period pursuant to §240.10D-1(b). ☐

Indicate by check mark whether the registrant is a shell company (as defined in Rule 12b-2 of the Act). Yes ☐ No ☒

As of June 30, 2025 (the last business day of the registrant's most recently completed second fiscal quarter), the aggregate market value of the registrant's common stock held by non-affiliates of the registrant was approximately $2.7 billion, based on the closing price of the registrant's common stock on the Nasdaq Global Select Market on such date of $28.76 per share.

The number of outstanding shares of the registrant's common stock, par value $0.001 per share, as of February 13, 2026 was 104,705,330.

DOCUMENTS INCORPORATED BY REFERENCE

Certain sections of the registrant's definitive proxy statement for the 2026 annual meeting of stockholders to be filed with the Securities and Exchange Commission pursuant to Regulation 14A not later than 120 days after end of the fiscal year covered by this Annual Report on Form 10-K are incorporated by reference into Part III of this Annual Report on Form 10-K.

GLOSSARY OF DEFINED TERMS

Unless expressly indicated or the context requires otherwise, the terms "Crinetics," "Company," "we," "us," and "our," in this Annual Report on Form 10-K (this "Report") refer to Crinetics Pharmaceuticals, Inc., a Delaware corporation, and, where appropriate, its wholly-owned subsidiaries. We also have used several other terms in this Report, most of which are explained or defined below.

"2024 Sales Agreement" means the Sales Agreement by and between Crinetics and the Sales Agents, dated June 21, 2024.

"A4" means androstenedione.

"ASD" means acromegaly symptom diary.

"ACTH" means the adrenocorticotrophic hormone.

"ADCS" means ACTH-Dependent Cushing's Syndrome.

"AMP" means average manufacturer price.

"ANDA" means abbreviated new drug application.

"Bayh-Dole Act" means the Bayh-Dole Act of 1980.

"CAH" means congenital adrenal hyperplasia.

"CAPL" means Crinetics Australia Pty Ltd, our wholly-owned subsidiary.

"CCPA" means the California Consumer Privacy Act.

"cGMP" means current Good Manufacturing Practice.

"CHMP" means the Committee for Medicinal Products for Human Use.

"CIO" means Chief Information Officer.

"CJEU" means the Court of Justice of the European Union.

"CMS" means the Centers for Medicare & Medicaid Services.

"CPRA" means the California Privacy Rights Act.

"CRF1" means corticotropin-releasing factor type 1.

"CRL" means a Complete Letter Response.

"CMOs" means contract manufacturing organizations.

"CROs" means contract research organizations.

"CS" means carcinoid syndrome.

"EC" means the European Commission.

"EEA" means the European Economic Area.

"EMA" means the European Medicines Agency.

"ESPP" means our 2018 Employee Stock Purchase Plan.

"Exchange Act" means the U.S. Securities Exchange Act of 1934, as amended.

"EU CTR" means the EU Clinical Trials Regulation.

"EU-U.S. DPF" means the Trans-Atlantic Data Privacy Framework.

"FDA" means the U.S. Food and Drug Administration.

"FDCA" means the federal Food, Drug, and Cosmetic Act.

"FDIC" means the Federal Deposit Insurance Corporation.

"GC" means glucocorticoid.

"GCP" means good clinical practice.

"GDPR" means the General Data Protection Regulation.

"GEP" means gastroenteropancreatic.

"GEP-NETs" means gastroenteropancreatic neuroendocrine tumors.

"GH" means growth hormone.

"GHRA" means growth hormone receptor antagonist.

"GPCRs" means G protein coupled receptors.

"Hatch-Waxman Amendments" means the Drug Price Competition and Patent Term Restoration Act of 1984.

"HC" means hydrocortisone.

"HIPAA" means the federal Health Insurance Portability and Accountability Act of 1996.

"IGF-1" means growth factor-1.

"IND" means Investigational New Drug.

"IPR" means inter partes review.

"IRA" means the Inflation Reduction Act of 2022.

"IRBs" means institutional review boards.

"IRP" means the International Recognition Procedure.

"Loyal" means Cellular Longevity Inc., doing business as Loyal.

"Loyal License" means the license agreement entered into with Loyal on March 24, 2023.

"MAA" means marketing authorization application.

"MHRA" means the United Kingdom Medicines and Healthcare products Regulatory Agency.

"MMAE" means monomethyl auristatin E.

"Nasdaq" means the Nasdaq Global Select Market.

"NDA" means new drug application.

"NDC" means nonpeptide drug conjugate.

"NECs" means neuroendocrine carcinomas.

"NENs" means neuroendocrine neoplasms.

"NETs" means neuroendocrine tumors.

"NIDDK" means the National Institute of Diabetes and Digestive and Kidney Diseases.

"NIH" means the National Institutes of Health.

"OLE" means open-label extension.

"ODD" means Orphan Drug Designation.

"PALSONIFY™®" means paltusotine for treatment of acromegaly in the U.S.

"PDUFA" means the Prescription Drug User Fee Act.

"PFS" means progression-free survival.

"PGR" means post-grant review.

"PK" means pharmacokinetics.

"PREA" means the Pediatric Research Equity Act.

"Privacy Shield" means the EU-US Privacy Shield Framework.

"PRRT" means peptide receptor radionuclide therapy.

"R&D" means research and development.

"Radionetics" means Radionetics Oncology, Inc.

"Radionetics License" means the collaboration and license agreement entered into with Radionetics in October 2021.

"REMS" means risk evaluation and mitigation strategy.

"Sales Agents" means SVB Leerink LLC and Cantor Fitzgerald & Co.

"SKK" means Sanwa Kagaku Kenkyusho Co., Ltd.

"SKK Clinical Supply Agreement" means the clinical supply agreement entered into with SKK on June 14, 2022.

"SKK License" means the license agreement entered into with SKK on February 25, 2022.

"SBIR Grants" means Small Business Innovation Research Grants.

"SCCs" means standard contractual clauses.

"SCLC" means small-cell lung cancer.

"SRLs" means somatostatin receptor ligands.

"SST2" means the somatostatin receptor type 2.

"SSAs" means the somatostatin analogs.

"SEC" means the Securities and Exchange Commission.

"TED" means Thyroid Eye Disease.

"ULN" means the upper limit of normal.

"UPC" means the Unitary Patent Court.

"U.S." means United States.

"U.S. GAAP" means U.S. Generally Accepted Accounting Principles.

CRINETICS PHARMACEUTICALS, INC.
FORM 10-K — ANNUAL REPORT

For the Fiscal Year Ended December 31, 2025

Table of Contents

PART I

Forward-Looking Statements

This Annual Report on Form 10-K contains forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended, or the Securities Act, and Section 21E of the Securities Exchange Act of 1934, as amended, or the Exchange Act. All statements other than statements of historical facts contained in this Annual Report on Form 10-K, including statements regarding our future results of operations and financial position, business strategy, commercialization efforts, prospective products, product approvals, research and development costs, timing and likelihood of success, plans and objectives of management for future operations and future results of our products and anticipated products, are forward-looking statements. These statements involve known and unknown risks, uncertainties, assumptions, and other important factors that may cause our actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by the forward-looking statements, which may also be impacted by any or all of the Risk Factors, noted in this Report. This Annual Report on Form 10-K also contains estimates and other statistical data made by independent parties and by us relating to market size and growth and other data about our industry. This data involves a number of assumptions and limitations, and you are cautioned not to give undue weight to such estimates. In addition, projections, assumptions and estimates of our future performance and the future performance of the markets in which we operate are necessarily subject to a high degree of uncertainty and risk.

In some cases, you can identify forward-looking statements by terms such as “may,” “will,” “should,” “expect,” “plan,” “anticipate,” “could,” “intend,” “target,” “goal,” “aspire,”“project,” “lead to,” “contemplates,” “believes,” “estimates,”“predicts,”“forecast” “potential” or “continue” or the negative of these terms or other similar expressions. The forward-looking statements in this Annual Report on Form 10-K are only predictions. We have based these forward-looking statements largely on our current expectations and projections about future events and financial trends that we believe may affect our business, financial condition and results of operations. These forward-looking statements speak only as of the date of this Annual Report on Form 10-K and are subject to a number of risks, uncertainties and assumptions, including those described in Part I, Item 1A, “Risk Factors.” The events and circumstances reflected in our forward-looking statements may not be achieved or occur and actual results could differ materially from those projected in the forward-looking statements. Moreover, we operate in an evolving environment. New risk factors and uncertainties may emerge from time to time, and it is not possible for management to predict all risk factors and uncertainties. Except as required by applicable law, we do not plan to publicly update or revise any forward-looking statements contained herein, whether as a result of any new information, future events, changed circumstances or otherwise.

We use our registered trademark Crinetics and our pending trademark PALSONIFY™ in this Annual Report on Form 10-K. This Annual Report on Form 10-K also includes trademarks, tradenames and service marks that are the property of their respective owners. Use or display by us of other parties’ trademarks, trade dress or products is not intended to and does not imply a relationship with, or endorsements or sponsorship of, us by the trademark, trade dress or product or their respective owners. Solely for convenience, trademarks and tradenames referred to in this Annual Report on Form 10-K appear without the ® and ™ symbols, but those references are not intended to indicate, in any way, that we or the respective owners will not assert, to the fullest extent under applicable law, any and all rights to these trademarks and tradenames.

Summary of Risk Factors

An investment in our securities involves a high degree of risk. You should carefully consider the risks summarized in Item 1A, “Risk Factors,” included in this Report. These risks include, but are not limited to, the following:

- We have a limited operating history, have incurred significant operating losses since our inception and expect to incur losses. We may never become profitable or, if we achieve profitability, we may not be able to sustain it.
- We may require substantial additional financing to achieve our goals, and failure to obtain this necessary capital when needed on acceptable terms, or at all, could lead us to delay, limit, reduce, abandon or terminate our product development programs, commercialization efforts or other operations.
- Currently, our ability to become profitable primarily depends on the commercial success of paltulsotine, approved as PALSONIFY in the U.S., and while we have two other product candidates in clinical development, all of our other research programs are still in the preclinical or discovery stage. If we are unable to successfully commercialize PALSONIFY or successfully develop any product candidates or experience significant delays in doing so, our business will be materially harmed.

- We cannot assure you that we will be able to successfully discover and develop any additional product candidates.
- Preclinical and clinical drug development involves a lengthy and expensive process with an uncertain outcome, and the results of preclinical studies and early clinical trials are not necessarily predictive of future results. Our product candidates that we develop may not have favorable results in later clinical trials, if any, or receive regulatory approval, and we may choose to terminate development for strategic reasons.
- We may find it difficult to enroll and retain patients in our clinical trials given the limited number of patients who have the diseases for which our product candidates are being developed. If we encounter difficulties enrolling subjects in our clinical trials, our clinical development activities could be delayed or otherwise adversely affected.
- Use of our products and product candidates could be associated with side effects or adverse events during their development or commercialization, which could severely harm our business, reputation, prospects, operating results and financial condition.
- Our product candidates are subject to extensive regulation and compliance, which is costly and time consuming and which may cause unanticipated delays or prevent the receipt of the required approvals to commercialize our product candidates.
- We have conducted, and continue to conduct, clinical trials for our current product candidates outside of the U.S., and we may do so for our other product candidates. However, conducting trials outside of the U.S. exposes us to additional risks, which could materially harm our business.
- Initial, interim, topline and preliminary data from our clinical trials that we announce or publish from time to time may change as more patient data becomes available and is subject to audit and verification procedures that could result in material changes in the final data.
- We are subject to ongoing regulatory obligations and continued regulatory review, which may result in significant additional expense. Additionally, PALSONIFY and, if approved, our other product candidates, could be subject to labeling and other restrictions on marketing or withdrawal from the market, and we may be subject to penalties if we fail to comply with regulatory requirements or if we experience unanticipated problems.
- The commercial success of PALSONIFY and our other product candidates, if approved, will depend upon the degree of market acceptance by physicians, patients, health care payors and others in the medical community.
- The successful commercialization of PALSONIFY and, if approved, our other product candidates, will depend in part on the extent to which governmental authorities and health insurers establish coverage, adequate reimbursement levels and favorable pricing policies. Failure to obtain or maintain coverage and adequate reimbursement for our products could limit our ability to market those products and decrease our ability to generate revenue.
- We face competition from entities that have developed or may develop somatostatin agonist products and other competitive candidates. If these companies develop competing technologies or product candidates more rapidly than we do or their technologies are more effective, our ability to develop and successfully commercialize products may be adversely affected.
- The numbers of patients suffering from the rare endocrine diseases and endocrine-related tumors that we target is small and have not been established with precision. If the market opportunities for our products are smaller than we believe they are, our revenue may be adversely affected, and our business may suffer.
- We obtained regulatory approval from the FDA for PALSONIFY but have limited demonstration of conducting commercial activities.

- Our future growth may depend, in part, on our ability to operate in foreign markets, where we would be subject to additional regulatory burdens and other risks and uncertainties.
- We rely on third parties for raw materials, active pharmaceutical ingredients, and drug product intermediates for the manufacture of our product candidates for preclinical and clinical development both within the US and internationally and expect to continue to do so for the foreseeable future. This reliance on third parties increases the risk that we will not have sufficient quantities of our product candidates or products or such quantities at an acceptable cost or subject to tariffs, which could delay, prevent or impair our development or commercialization efforts.
- We are dependent on the services of our management and other clinical and scientific personnel, and if we are not able to retain these individuals or recruit additional management or clinical and scientific personnel, our business will suffer.
- Our success depends on our ability to protect our intellectual property and our proprietary technologies, and if we are unable to protect our intellectual property and technologies, our business will suffer.
- The trading price of the shares of our common stock could be highly volatile, and purchasers of our common stock could incur substantial losses.
- Raising additional capital may cause dilution to our stockholders, restrict our operations or require us to relinquish rights to our technologies or product candidates.
- Our operating results may fluctuate significantly, which makes our future operating results difficult to predict and could cause our operating results to fall below expectations or any guidance we may provide.
- Business disruptions could seriously harm our future revenue and financial condition and increase our costs and expenses.

Item 1. Business

Business Overview

We are a pharmaceutical company committed to transforming the treatment of endocrine diseases and endocrine-related tumors through science rooted in patient needs. We are focused on discovering, developing, and commercializing novel therapies, with a core expertise in targeting GPCRs with small molecules that have specifically tailored pharmacology and properties.

Our lead product, PALSONIFY (paltusotine), is the first once-daily, oral treatment approved by the FDA for the treatment of adults with acromegaly who had an inadequate response to surgery and/or for whom surgery is not an option. Paltusotine is also in clinical development for CS associated with NETs. Our deep pipeline of 10+ disclosed programs includes late-stage investigational candidate atumelnant, which is currently in development for CAH and ADCS, and CRN09682, a NDC candidate that is being developed to treat SST2 expressing NETs and other SST2 expressing solid tumors. Additional discovery programs address a variety of endocrine conditions such as NETs, Graves' disease (including Graves' hyperthyroidism and Graves' orbitopathy, or TED), polycystic kidney disease, hyperparathyroidism, diabetes, obesity, and GPCR-targeted oncology indications.

Approved Product

- On September 25, 2025, the FDA approved PALSONIFY as the first and only once-daily oral somatostatin receptor ligand for the treatment of adults with acromegaly who had an inadequate response to surgery and/or for whom surgery is not an option.

Key Pipeline Updates

Paltusotine

- The first patient was enrolled in the Phase 3 study of paltusotine for CS in November 2025.
- In February 2026, the CHMP of the EMA adopted a positive opinion, recommending the marketing authorization of PALSONIFY for the medical treatment of adult patients with acromegaly. The CHMP opinion will be reviewed by the EC, consistent with a timeline for a potential decision in the first half of 2026.

Atumelnant

- In January 2025, we reported positive results from the first three cohorts of the Phase 2 TouCAHn open-label study of atumelnant in CAH. In January 2026, we provided an update, including data on the fourth cohort of the Phase 2 TouCAHn study and data from the separate OLE study. Participants in all four cohorts were eligible to enroll in the OLE.
- In May 2025, we announced the design of our Phase 3 CALM-CAH study. The first participant in the CALM-CAH study was randomized in December 2025.
- In August 2025, we announced our pediatric trial design in CAH, BALANCE-CAH. BALANCE-CAH is designed as an operationally seamless Phase 2/3 study. The first participant in the BALANCE-CAH study was dosed in January 2026.
- We expect to initiate an operationally seamless Phase 2/3 study of atumelnant in ADCS (EQUILIBRIUM-ADCS) in the first half of 2026.

CRN09682

- In April 2025, we received IND clearance for CRN09682, the first candidate from the NDC platform. In November 2025, the first patient received CRN09682 in the dose escalation phase of a Phase 1/2 study.

Our Strategy

Our mission is to build the world's leading endocrine company that pioneers new therapeutics to help patients better control their disease and improve their daily lives. To achieve this mission, we are pursuing the following strategy:

- ***Commercialize our product candidates.*** PALSONIFY became the first oral nonpeptide SST2-agonist approved by the FDA for the treatment of acromegaly in September 2025 and was commercially available in October 2025 in the U.S. We are establishing a highly specialized and focused commercial organization, including sales, marketing and market access expertise to support the launch of PALSONIFY in the U.S. We continue to execute our launch strategy by educating healthcare providers and patients on the diagnosis and appropriate clinical management of acromegaly and the potential clinical benefits and appropriate use of PALSONIFY.
    - We are also activating patients to request PALSONIFY, educating HCPs on PALSONIFY to drive breadth and depth of prescribers and engaging with payers to support patient access to therapy and formulary inclusion of PALSONIFY. We believe PALSONIFY's profile as a once-daily, oral SST2R agonist that is approved to offer biochemical and symptom control and convenience will provide meaningful differentiation in the acromegaly competitive landscape.
    - We are building the structure and expertise to commercialize our product candidates in additional markets, including the EU, where we believe we can do this efficiently and effectively, if approved by regulators. In February 2022, we entered into the SKK License pursuant to which SKK has the exclusive right to commercialize paltusotine in Japan. In the future, we may seek relationships with additional global licensing, distribution or other partners for our product candidates where we determine this to be an effective approach.
- ***Focus on endocrine diseases and endocrine-related tumors with significant unmet medical need.*** There are numerous endocrine diseases and endocrine-related tumors for which currently available pharmacological therapies (when they exist) have significant limitations in efficacy, safety and/or tolerability. Patients living with these diseases often experience significant morbidity, mortality and/or poor quality of life. We are focused on discovering, developing, and commercializing therapies for multiple indications across endocrinology to advance the standard of care for these patients.
- ***Rapidly advance multiple product candidates in parallel to clinical proof-of-concept and late-stage development by targeting diseases that employ validated biomarkers as clinical endpoints.*** Phase 1 clinical trials for endocrine diseases and endocrine-related tumors can often measure predictive biomarkers in healthy volunteers and lower the technical risk by providing a predictive measure of efficacy early in clinical development.
- ***Continue to expand our therapeutic pipeline for endocrine diseases and endocrine-related tumors by leveraging the capabilities of our experienced discovery team in the area of peptide hormone GPCRs.*** Our discovery team has significant expertise in understanding and creating product candidates to influence the dynamic behavior of GPCRs and has developed a number of proprietary methods, techniques and tools that we

believe will enable us to efficiently and reliably evaluate newly synthesized molecules. We employ an iterative strategy where compounds are designed, synthesized, and rapidly characterized for pharmacologic and pharmaceutical properties. This approach has led to our current pipeline, and we will continue to invest in creating additional product candidates acting at this important class of targets. Peptide hormone GPCRs regulate many aspects of physiology and are attractive drug targets for treating a broad range of diseases. There are more than 80 known peptide hormones acting at more than 120 known different receptors. With each of our drug discovery programs, our goal is to specifically tailor a product candidate with pharmacologic and pharmaceutical properties highly optimized for its interaction with its specific GPCR target that we anticipate will translate to downstream benefits in our chosen therapeutic applications. For example, the SST2R ligand in paltusotine is designed to disfavor internalization of SST2R, while the SST2R ligand in CRN09682 is designed to promote internalization.

- ***Maintain an entrepreneurial, scientifically rigorous, and inclusive corporate culture where employees are fully engaged and strive to bring improved therapeutic options to patients.*** The patients we seek to treat often have limited treatment options with significant drawbacks and often limited efficacy, safety and/or tolerability. We are passionate about developing new pharmacological therapies to help these patients better control their diseases and to reduce the impact of these diseases on their daily lives. We believe that building a successful and sustainable endocrine company requires not just specific expertise in multiple areas of drug discovery, development, and commercialization, but a team-oriented culture that integrates and harnesses the creative energy, scientific insights and passion of the entire organization.

The Endocrine System

Overview

The endocrine system regulates most of the body's physiological activities through the actions of hormones, which are chemical and biochemical messengers secreted from different organs that influence growth, gastrointestinal function, maturation and development, reproduction, stress, metabolism and nearly all aspects of homeostasis. Hormonal dysregulation can arise from endocrine organ defects, including injury, inflammation, genetic abnormalities, or the growth of tumors derived from endocrine cells. These insults can result in the under-secretion or over-secretion of one or more hormones, disrupting homeostasis and causing disease. For example, several serious clinical disorders, including acromegaly and Cushing's disease, result from pituitary tumors secreting excess hormones.

Peptide hormone GPCRs

Various GPCRs are expressed in every type of cell in the body and their function is to transmit signals from outside the cell across the membrane to signaling pathways within the cell, between cells and between organ systems. Because of these critical actions, the GPCR superfamily is the largest and single most important family of drug targets as highlighted by the large number of approved therapeutics targeting this class. However, most currently available GPCR-targeting drugs act as receptors for which the native ligands are small molecules, such as histamine, adrenaline, and neurotransmitters.

Most peptide hormones bind selectively to specific receptors located on the surface of cells in the target tissue. Receptors for peptide hormones are often GPCRs, which play a central role in many biological processes and are linked to a wide range of disease areas. There are more than 80 known peptide hormones acting at more than 120 known different receptors. Historically, it was assumed that small molecules could not replicate or compete with the complex interactions between peptides and their cognate GPCRs. As such, most drugs developed for peptide GPCRs have been and continue to be peptides themselves, which present manufacturing and formulation difficulties and force patients to undergo frequent injections because peptides generally are not orally bioavailable. We believe our approach to developing novel small molecule product candidates that uniquely engage peptide hormone GPCRs will enable us to generate orally bioavailable, and potentially more selective, effective and better tolerated therapeutics for patients.

GPCRs were originally thought to function as simple on-off switches responding to hormones and neurotransmitters but have since been shown to exhibit complex and diverse molecular and cellular behaviors. Many lines of structural and mechanistic research demonstrate that distinct signaling cascades and feedback mechanisms create multi-dimensional pathways with distinct physiological responses. These different responses are based on ligand binding kinetics, receptor regulation and trafficking. Some transduce signals into the cell interior to regulate various cellular functions. Other responses attenuate hormonal signals to prevent overstimulation and include receptor internalization (a removal of the GPCR from the cell surface, which makes it unavailable for external ligands), desensitization and downregulation. We believe our understanding of these different signaling pathways enables us to develop oral, small molecule product candidates that not only are highly selective for specific receptor subtypes but also are further custom-tailored to activate specific GPCR properties and ultimately improve patient outcomes.

Product Pipeline Summary

All of our product candidates have been discovered and developed internally and we have retained global rights to commercialize our product candidates and have no royalty or licensing obligations, other than the licenses and collaborations discussed under "Our Strategic Collaborations" herein.

The following table summarizes our current product candidate pipeline.

Our Products and Product Candidates

We focus on the discovery and development of nonpeptide therapeutics that target peptide GPCRs with well-understood biological functions, validated biomarkers and the potential to substantially improve the treatment of endocrine diseases and endocrine-related tumors.

Paltusotine (SST2 Agonist Program)

Acromegaly Disease Background

Acromegaly is a serious chronic endocrine disorder typically caused by a pituitary tumor that secretes excess GH. Pituitary tumors are generally benign adenomas that, in addition to GH secretion, also express membrane receptors for somatostatin. Increased GH secretion results in excess downstream secretion of IGF-1 from the liver. GH and IGF-1 promote tissue growth and have other metabolic effects throughout the body.

The consequences of chronically elevated GH and IGF-1 can be severe, including changes in facial features, enlargement of the hands and feet, and carpal tunnel syndrome. Enlargement of the heart can lead to congestive heart failure and these excess hormones also induce insulin resistance, hypertension, and other negative clinical consequences.

From the perspective of someone living with acromegaly, the physical changes in their appearance, not to mention the sweating and skin changes, can be alarming and socially isolating. Severe headaches, fatigue, joint pain, and peripheral neuropathies can be debilitating. Additional symptoms can include thick, coarse, oily skin, skin tags, excessive sweating and skin odor, fatigue and weakness, headaches, goiter, decreased libido, menstrual abnormalities in women and erectile

dysfunction in men. As the tumor grows, it can impinge on the nerves in the optic chiasm leading to visual problems and potentially vision loss. Compression of the surrounding normal pituitary tissues can decrease production of other pituitary hormones, resulting in hypopituitarism. Acromegaly patients experience increased mortality rates, principally due to cardiovascular diseases (diabetes, hypertension), respiratory disease and cerebrovascular diseases.

Acromegaly is often suspected when the patient exhibits enlargement of extremities and an alteration of facial features. Pituitary tumors are also often found during clinical workup for severe headaches, vision changes or incidentally on cranial imaging initiated for other reasons. Elevation of serum IGF-1 levels confirms the suspicion of acromegaly, but a formal diagnosis requires lack of suppression of serum GH levels in response to an oral glucose tolerance test. A magnetic resonance imaging (MRI) or computerized tomography (CT) scan of the pituitary is then used to locate the tumor, determine its size and assess the potential for surgical intervention. Unfortunately, for many patients, it can take 5 to 10 years to reach a diagnosis.

Our research suggests that there are approximately 36,000 people living with acromegaly in the U.S., of which 17,000 or more are undiagnosed, 7,500 are not in active follow-up for treatment, and 11,500 are actively managed. Our research further suggests that of the 11,500 actively managed patients in the U.S., 40% are treatment naïve, 25% are on injectable somatostatin receptor ligands, 20% are on other therapies, and 15% have discontinued treatment. Our research also indicates that there are approximately 1,500 newly diagnosed patients per year, 500 of which are candidates to initiate pharmaceutical treatment.

Acromegaly Clinical Development Program

PALSONIFY, is the first once-daily, oral treatment approved by the FDA in the U.S. for the first-line treatment of adults with acromegaly who had an inadequate response to surgery and/or for whom surgery is not an option. Paltusotine is also in clinical development for CS associated with neuroendocrine tumors.

Paltusotine establishes a new class of oral selective nonpeptide SST2 agonists designed for the treatment of adults with acromegaly and CS due to well-differentiated neuroendocrine tumors. Somatostatin is a neuropeptide hormone that broadly inhibits the secretion of other hormones, including GH from the pituitary gland.

Our Phase 3 development program for paltusotine in acromegaly consisted of two placebo-controlled clinical trials, PATHFNDR-1 and PATHFNDR-2. The PATHFNDR-1 trial was designed as a double-blind, placebo-controlled, nine-month clinical trial of paltusotine in acromegaly patients with average IGF-1 levels less than or equal to 1.0 times the ULN and who had been on stable doses of somatostatin receptor ligand monotherapy (octreotide LAR or lanreotide depot). We also conducted a second study, the PATHFNDR-2 trial, which was designed as a double-blind, placebo-controlled, six-month clinical trial of acromegaly patients who were not on pharmacological treatment and had elevated IGF-1 levels. The primary endpoint of both PATHFNDR studies was the proportion of patients with IGF-1 $\leq$ 1.0 ×ULN at the end of the treatment period on paltusotine as compared to placebo.

Positive topline data from the randomized controlled portion of the PATHFNDR-1 study was reported in September 2023, where the primary endpoint and all secondary endpoints of the study were achieved. Additionally, in the PATHFNDR-1 study, paltusotine was well tolerated and no serious or severe adverse events were reported in participants treated with paltusotine.

In March 2024, we reported positive topline results from the PATHFNDR-2 study. The study met statistical significance ($p<0.0001$) on the primary endpoint, and all secondary endpoints. Additionally, in PATHFNDR-2, paltusotine was generally well-tolerated and no serious adverse events were reported in participants treated with paltusotine.

The OLE phases of both PATHFNDR trials are ongoing. In July 2025, we presented open-label extension data from both the pivotal PATHFNDR-1 and PATHFNDR-2 trials in two presentations, showing the long-term clinical profile of PALSONIFY in people with acromegaly.

Data from the PATHFNDR-1 OLE demonstrated that mean insulin-like IGF-1 levels remained stable with IGF-1 (mean ± SE) of 0.93 ± 0.22 at OLE baseline and 0.81 ± 0.21 times the ULN at Week 96, demonstrating durable biochemical control over this time span. Symptom control, as measured by the ASD, and GH level also remained stable at Week 96. PALSONIFY was generally well tolerated.

Data from the PATHFNDR-2 OLE demonstrated that patients with placebo during the RC portion of the study and then transitioned to paltusotine experienced sustained reductions in IGF-1, with a mean change from baseline of –0.81 × ULN at Week 84 (n=39). Direct-to-OLE participants (n=9) showed similar reductions (–0.75 × ULN), while those who had been treated with PALSONIFY during the RC phase (n=40) maintained control (mean change –0.01 × ULN). GH, ASD symptom scores and pituitary tumor size were durably controlled over the study period. PALSONIFY was generally well tolerated.

On September 25, 2025, the FDA approved PALSONIFY for the first-line treatment of adults with acromegaly who had an inadequate response to surgery and/or for whom surgery is not an option. The FDA has granted orphan drug designation for paltusotine for the treatment of acromegaly. We believe that the results of the clinical trials of paltusotine could support marketing applications outside the U.S. for the use of paltusotine for all acromegaly patients who require pharmacotherapy, including untreated patients and those switching from other therapies.

In February 2025, the EMA, granted paltusotine orphan drug designation for the treatment of acromegaly. Designation was given following a positive recommendation from the EMA Committee for Orphan Medicinal Products, highlighting the potential impact of paltusotine for acromegaly patients in the European Union. The EMA validated the MAA in March 2025. The EMA also granted ODD for paltusotine for the treatment of acromegaly, further highlighting the level of unmet need and the potential for paltusotine to offer significant benefit to patients. In February 2026, CHMP of the EMA adopted a positive opinion, recommending the marketing authorization of PALSONIFY for the medical treatment of adult patients with acromegaly. The CHMP opinion will be reviewed by the EC, consistent with a timeline for a potential decision in the first half of 2026. Paltusotine is also in development for acromegaly in Japan through our licensing agreement with SKK.

To date, our clinical trials have shown that paltusotine was generally well tolerated among healthy adults and patients with acromegaly.

CS Disease Background

NENs are comprised of NECs, which are poorly differentiated and highly proliferative, with rapid disease progression; and NETs, which are well differentiated and generally slow-growing. NETs represent 80-90% of NENs and include tumors with a broad range of disease characteristics depending on site, grade and other features. NETs most commonly originate from the gastrointestinal tract, lungs and pancreas, and approximately 75% of NETs express SST2 receptors, with higher rates of expression in well-differentiated NETs.

Many NETs are well differentiated and exhibit indolent growth, frequently remaining asymptomatic for prolonged periods. As a result, a significant proportion of patients are diagnosed at an advanced or metastatic stage, often with liver metastases that can drive morbidity and mortality. A subset of NETs are functional, meaning they secrete hormones or other biologically active substances and are associated with corresponding symptoms. Approximately one-fifth of NETs cases are associated with excess serotonin secretion, leading to CS. The key debilitating symptoms of CS are cutaneous flushing (>90% of cases) and chronic diarrhea (60-80% of cases). Patients with CS may also present with related systemic symptoms, including mesenteric fibrosis, abdominal pain, carcinoid heart disease and other symptoms.

We estimate that 28,000-51,000 adults diagnosed with NETs are undergoing medical management. Of these, it is estimated that approximately 18,000-34,000 are candidates for treatment with paltusotine, if it is approved for the treatment of CS.

CS Clinical Development Program

In March 2024, we reported positive topline results from our randomized, open-label, parallel group, multi-center Phase 2 study to assess safety, tolerability, pharmacokinetics, and efficacy of paltusotine in people living with CS. A total of 36 participants were randomized to receive either 40 mg (n=18) or 80 mg (n=18) of paltusotine for eight weeks, with the ability to adjust dose based on tolerability or inadequate control of symptoms during the first four weeks of treatment. Results demonstrated that administration of paltusotine resulted in rapid and sustained reductions in bowel movement frequency and flushing episodes. Paltusotine was generally well-tolerated with a safety profile consistent with prior clinical studies, with no treatment-related severe or serious adverse events.

Patients from the Phase 2 study were eligible to enroll in an open-label extension study of paltusotine in CS. In November 2025, we shared one-year investigator-assessed PFS data from the open-label study, which showed a PFS rate of 74% following one year of treatment.

The Phase 3 CAREFNDR study is designed to evaluate the safety and efficacy of paltusotine in patients with CS. The first patient in the CAREFNDR study was dosed in November 2025 and we continue to activate additional sites. CAREFNDR is designed as a double-blind, placebo-controlled, sixteen-week clinical trial to enroll CS patients (who may or may not be on pharmacological treatment at baseline) and are actively symptomatic. The primary endpoint of the CAREFNDR trial is the percentage change from baseline in the frequency of flushing episodes at week 12. In addition, a key secondary endpoint measures the change from baseline in bowel movement frequency at week 12. The CAREFNDR trial is designed to capture other efficacy endpoints including severity of flushing and urgency of bowel movements. Following the 16-week randomized controlled period, the trial will include a 104-week OLE to evaluate long-term efficacy, safety and additional clinical outcomes. The OLE will include an exploratory assessment of tumor control.

To date, our clinical trials have shown that paltusotine was generally well tolerated among healthy adults and patients with CS.

Atumelnant (ACTH Antagonist)

Atumelnant is our investigational, orally available, nonpeptide product candidate designed to block the action of ACTH on the ACTH receptor. It is intended for the treatment of diseases caused by excess ACTH, including CAH and ADCS, which includes patients with either Cushing's disease or EAS.

We conducted a double-blind, randomized, placebo-controlled Phase 1 study of atumelnant in healthy volunteers to assess the safety and tolerability of single and multiple doses of atumelnant. In addition, the study was designed to measure the effect of atumelnant on suppression of cortisol, cortisol precursors, and adrenal androgens following exogenous ACTH stimulation. In May 2022, we announced positive topline data from the Phase 1 study in healthy volunteers which showed atumelnant was well tolerated and demonstrated dose-dependent increases in atumelnant plasma concentrations. We believe atumelnant demonstrated pharmacologic proof-of-concept, as the Phase 1 results showed dose-dependent reductions of both basal cortisol and elevated cortisol following an ACTH challenge. All adverse events were considered mild to moderate and there were no serious adverse events.

CAH encompasses a set of disorders that are caused by genetic mutations that result in impaired cortisol synthesis. A lack of cortisol leads to a breakdown of feedback mechanisms and results in persistently high levels of ACTH, which, in turn, causes overstimulation of the adrenal cortex. The resulting adrenal hyperplasia and over-secretion of other steroids (particularly androgens) and steroid precursors can lead to a variety of effects from improper gonadal development to life-threatening dysregulation of mineralocorticoids. We estimate that approximately 17,000 patients are potential candidates for treatment with atumelnant, 12,000 of which are adults and 5,000 of which are pediatric.

Cushing’s disease results from a pituitary tumor that secretes excess ACTH, and EAS results from non-pituitary ectopic tumors which secrete ACTH. The excess secretion of ACTH causes the downstream synthesis and over-secretion of cortisol by the adrenal glands. Cortisol is the body’s main stress hormone and excess amounts can cause significant increases in mortality and morbidity. We estimate there are over 11,000 patients with Cushing’s disease in the U.S., of which approximately 5,000 patients are potential candidates for treatment with atumelnant.

CAH Disease Background

CAH encompasses a set of disorders that are caused by genetic mutations that result in impaired cortisol synthesis. This lack of cortisol leads to a breakdown of feedback mechanisms and results in persistently high levels of ACTH, which in turn causes overstimulation of the adrenal cortex. The resulting adrenal hyperplasia and over-secretion of other steroids (particularly androgens) and steroid precursors can lead to a variety of effects from improper gonadal development to life-threatening dysregulation of mineralocorticoids. CAH patients have a two-fold risk of bone fractures compared to the general population and commonly suffer from hypercholesterolemia, insulin resistance, and hypertension. Compared to the general population, CAH patients have a diminished life expectancy of 7 years, and more than 20% of CAH patients will die of a condition complicated by adrenal crisis.

Treatment goals for adults with CAH include:

- Reduce A4 and other androgens to address hyperandrogenism, which can manifest as excessive facial hair, acne and polycythemia;
- Restore normal menstrual cycles and fertility in women;
- Shrink testicular adrenal rest tumors, alleviate pain and restore fertility in men; and
- Eliminate excessive exposure to glucocorticoids to minimize steroid therapy related adverse effects including weight gain, cardiovascular issues, diabetes, and osteoporosis.

CAH is an orphan indication with an estimated prevalence of approximately 17,000 patients in the U.S., of which 12,000 are adult and 5,000 are pediatric.

CAH Clinical Development Program

We conducted the TouCAHn Phase 2 study of atumelnant in adult CAH patients. This open-label study was designed to evaluate the safety, efficacy, and pharmacokinetics of different doses of atumelnant. In addition, biomarkers, including serum A4 and 17 hydroxyprogesterone (17-OHP), were measured to evaluate the potential efficacy of atumelnant. We reported positive initial findings from our Phase 2 study in June 2024 and topline data from 28 patients in January 2025. Atumelnant administration was shown to result in rapid, substantial and sustained statistically significant reduction in A4 levels, the key biomarker for disease control, and demonstrated significant clinical improvements. Atumelnant demonstrated statistically significant reductions of A4 at the first 2-week time point in all dose groups (40 mg, 80 mg, and 120 mg). These effects were sustained through the 12-week prespecified primary endpoint where the degree of suppression

was dose dependent and statistically significant. The data showed that atumelnant was well-tolerated with no treatment-related severe or serious adverse events.

We have continued progress on the development program for atumelnant across multiple trials. In January 2026, we presented additional data from the Phase 2 study of atumelnant in adults with CAH. The update included data from the fourth cohort (n=10, 12-week study); two participants withdrew consent for administrative reasons. The participants received atumelnant (80 mg) once daily in the morning and underwent GC dose reduction toward physiologic levels (<11 mg/m^2/day HC or equivalent) in weeks 2 to 10. Treatment with atumelnant resulted in rapid, sustained lowering of A4 (in all 8 patients that completed the fourth cohort). Seven out of these 8 patients continued to maintain lower A4 after glucocorticoid doses were reduced to physiologic levels. Atumelnant was well-tolerated with no serious adverse events and no treatment-related severe adverse events. No participants discontinued due to adverse events. No patients experienced hepatic transaminase adverse events. Participants from this study were given the option to enroll in our open-label extension study.

We have initiated a Phase 3 study (CALM-CAH) in adult CAH patients, with first participant randomized in December 2025. The study has an uncompromising primary endpoint to demonstrate atumelnant's potential ability to normalize A4 levels while patients are on physiological doses of GC replacement. CALM-CAH is designed as a Phase 3 double-blind, placebo-controlled, thirty two-week clinical trial to enroll patients with CAH. The primary endpoint of the CALM-CAH trial is the proportion of participants with A4 ≤ULN (upper limit of normal) who are on physiologic GC replacement at week 32. The CALM-CAH trial is also designed to evaluate the impact of atumelnant on the clinical signs, symptoms, co-morbidities and outcomes of CAH. The participants in the CALM-CAH can roll into the open-label extension study referenced above.

In January 2026, we presented a data snapshot with limited source data verification from the first 7 patients in the OLE to have completed at least 13 weeks. Those data showed both serum A4 reductions and GC dose reductions that were in line with those seen in Cohort 4. Additionally, investigators have not observed any serious adverse events or any treatment-related severe adverse events, and have not observed any hepatic transaminase adverse events to date with 25 patients enrolled and with 7 participants who have completed over 20 weeks of treatment in the study.

The BALANCE-CAH pediatric study is a seamlessly-operational Phase 2/3 study, and the first patient was dosed in January 2026. The Phase 2 is an open-label, semi-sequential cohort study to evaluate the safety, efficacy, and PK of atumelnant treatment in pediatric participants with classic CAH. The Phase 3 is a double-blind, placebo-controlled confirmatory portion of the study to evaluate the safety and efficacy of atumelnant in pediatric participants with classic CAH. Pediatric participants that completed participation in either Phase 2 or Phase 3 of this study will be eligible to enroll in the OLE, a single-arm, open-label, long-term safety and efficacy study. The primary endpoint in the Phase 2 portion is change from baseline in morning serum A4 at Week 8, and the primary endpoint in the Phase 3 portion is the percent change from baseline in GC daily dose at Week 28 while serum early morning A4 is less than the upper limit of normal.

ACTH-Dependent Cushing's Syndrome Disease Background

Cushing's syndrome results from a prolonged exposure to elevated levels of glucocorticoids, particularly cortisol. Common signs include growth of fat pads (above the collarbone and on back of the neck), abdominal obesity, facial fat accumulation, excessive sweating, dilation of capillaries, thinning of the skin, muscle weakness, hirsutism, depression/anxiety, hypertension, osteoporosis, insulin resistance and hyperglycemia, heart disease and a range of other metabolic disturbances resulting in high morbidity. While excessive synthetic steroid administration or adrenal tumors can cause ACTH-independent forms of the disease, ACTH dependent Cushing's syndrome (which includes Cushing's disease and Ectopic ACTH Syndrome) is the most common form, accounting for 60-80% of all cases. Cushing's disease is caused by tumors of pituitary corticotroph cells that secrete excess ACTH. EAS is caused by tumors outside the pituitary gland that secrete excess ACTH.

EAS is a rare disorder that results from non-pituitary tumors that secrete excessive amounts of ACTH. The supraphysiological degree of ACTH secretion in EAS can vary with effects that range from cushingoid to acutely life-threatening. Treatment options for EAS are limited, with the first goal being surgical removal of the tumors, if possible. If surgery is not an option, medical therapy may be used to block cortisol production. And in some cases, adrenalectomy is required if the tumor cannot be located and medical therapy does not fully block the cortisol.

Cushing's disease is an orphan indication with a prevalence of approximately 11,000 patients in the U.S. It presents more commonly in women, and usually between 30 and 50 years of age. Cushing's disease often takes many years to diagnose and may well be under-diagnosed in the general population as many of its symptoms such as lethargy, depression, obesity, hypertension, hirsutism and menstrual irregularity can be incorrectly attributed to other more common disorders.

ACTH-Dependent Cushing's Syndrome Clinical Development Program

Atumelnant is currently being studied in patients with ADCS, including those with Cushing's disease and Ectopic ACTH Syndrome, in an open-label, multiple-ascending dose Phase 1b/2a trial. This single-center, in-patient study is in collaboration with the NIDDK of the NIH. The ten-day study is designed to evaluate safety, tolerability, and pharmacokinetics of different doses of atumelnant in patients with ADCS as well as to measure 24-hour urinary-free cortisol and serum cortisol as indicators of efficacy. We reported positive initial findings from the study in June 2024, and the study remains ongoing. We expect to initiate an operationally seamless Phase 2/3 study of atumelnant in ADCS (EQUILIBRIUM-ADCS) in the first half of 2026. The Phase 2 is a double-blind, placebo-controlled study, and will inform dose selection for the Phase 3 double-blind placebo-controlled part of the study. Participants that participate in either the Phase 2 or Phase 3 portion will be eligible to enroll in the OLE, a single-arm, open-label, long-term safety and efficacy part of the study.

CRN09682 (non-peptide drug conjugate for SST2 positive solid tumors)

We have developed a first-in-class, non-peptide, non-radioactive NDC linking an SST2 agonist with the cytotoxic drug MMAE, via a spacer and a cleavable linker for the treatment of NETs and potentially for use in other solid tumors that express SST2, or SST2+ tumors. CRN09682 is designed to selectively deliver MMAE to SST2-expressing tumor cells, such that the delivery of MMAE is directed to the SST2 expressing tumors to drive antitumor activity, while minimizing the uptake of the conjugate in other tissues that do not express or express low levels of SST2.

Measurement of CRN09682 and MMAE levels in tumor tissues from mice bearing small-cell lung cancer (NCI-H524 SCLC CDX) demonstrated high tumor uptake for CRN09682 and prolonged MMAE tumor exposure, relative to MMAE in plasma and CRN09682 in plasma. These in vitro data suggest that CRN09682 inhibits cancer cell proliferation upon selective SST2 activation and internalization of CRN09682.

SST2-Positive Solid Tumor Disease Background

NENs arise across multiple organs and vary widely in behavior, with treatment guided by tumor grade and differentiation. Disease severity ranges from well-differentiated, indolent NETs to poorly differentiated, highly aggressive NECs, including SCLC. Well-differentiated tumors generally exhibit higher SST2 expression and are often associated with better outcomes. Approximately 75% of NET patients express SST2, with higher, more consistent expression in well-differentiated, low-grade, and GEP-NETs. Poorly differentiated NECs typically exhibit lower SST2 expression and are linked to more aggressive disease and poorer prognoses.

NENs often present at advanced, incurable stages, with more than half of cases metastatic, typically to the liver. They are classified as functional or nonfunctional based on symptoms or hormone hypersecretion; for example, CS results from excess serotonin production.

Patients with locoregional and resectable tumors often undergo surgery as a first step. Those with metastatic or unresectable tumors may undergo medical management for symptom and/or tumor control. Medical management may commonly include SSAs, PRRT, chemotherapy, or kinase / mTOR inhibitors.

We estimate that 28,000 to 51,000 patients with NENs receive medical management, of which an estimated 11,000 to 21,000 seek treatment for tumor control and represent the initial addressable population for CRN09682. Additional SST2-expressing tumors—such as SCLC, meningioma, head and neck cancer, and breast cancer—may further expand the number of patients who could benefit from CRN09682.

SST2-Positive Solid Tumors Clinical Development Program

We received IND clearance for CRN09682, the first candidate from our NDC platform, along with a "Study May Proceed" letter authorizing initiation of a Phase 1/2 study in metastatic or locally advanced SST2-positive neuroendocrine tumors and other SST2-expressing solid tumors. In November 2025, the first patient was dosed in our BRAVESST2 Phase 1/2 study.

During the Phase 1 dose-escalation stage, we plan to enroll 3–6 patients per ascending dose cohort until the maximum tolerated dose is established. Results from this stage will guide selection of the recommended expansion dose for Phase 2 and determine the tumor sub-types to include in the expansion cohorts. Across both phases, we expect to enroll up to 150 participants.

Early Stage Product Pipeline Summary

In addition to our clinical stage pipeline, we have several preclinical candidates in development. We may provide updates on these molecules from time to time or if and when they have received IND clearance.

Research Discovery

Patients with many other debilitating endocrine diseases and endocrine related tumors await new therapeutic options, and we continuously evaluate and prioritize where to deploy our drug discovery efforts. We plan to continue to expand our drug discovery efforts and leverage our expertise in the evaluation of additional unmet medical needs. Our drug discovery and development efforts are focused on endocrine, metabolism, and targeted therapies.

Endocrine: Our deep understanding of endocrine systems and patient needs have produced a robust pipeline of transformative novel molecules that are purposefully designed to meet the needs of patients. We focus on developing innovative nonpeptide drug candidates with unique methods of action, targeting particular endocrine pathways, including non-traditional ones, where modulating irregular hormone secretion can lead to improving conditions that significantly impact patients' lives.

Metabolism: Metabolic disorders including diabetes, obesity, and others impact the lives of hundreds of millions of people across the world and their effects on patients are significant and varied. Many of these disorders are a result of the dysregulation of key metabolic hormones, including insulin, glucagon, glucagon-like peptide-1, gastric inhibitory polypeptide, and others. Crinetics' understanding of these hormonal pathways and the GPCRs that control them coupled with our expertise in developing nonpeptides with specific pharmacologies allows us to create new molecules with the chance to improve the lives of patients with metabolic diseases.

Targeted Therapies: Our efforts in precision oncology began with developing nonpeptide, GPCR-targeted radioligands for the imaging and treatment of a broad range of endocrine receptor-driven cancers, ultimately leading to the formation of Radionetics in 2021. Our continued dedication to this concept has led to our latest novel development program that is exploring a new modality known as NDCs, a unique therapeutic approach that leverages endocrine receptors for highly selective targeting of anti-tumor agents.

Product Competition for Clinical Stage Candidates

The commercialization of new drugs is competitive, and we could face competition from a number of pharmaceutical or biotechnology companies around the world. Our commercial opportunity could be reduced or eliminated if our competitors develop and commercialize products that are safer, more effective, have fewer or less severe side effects or are more convenient than any products that we may develop. Our competitors also may obtain FDA or other regulatory approval for their products more rapidly than we do. The key competitive factors affecting the success of all of our programs are likely to be their efficacy, safety and convenience. See "Risk Factors – Risks related to commercialization of PALSONIFY and our product candidates."

Acromegaly

The major goals of treatment are to reduce serum GH and normalize IGF-1 levels, ameliorate symptoms, and reduce or stabilize the pituitary tumors that cause acromegaly. Surgical removal of the pituitary tumor is usually the first treatment and can result in long-term remission if the tumor is fully resected. For those for whom surgery is not an option and those whose tumors are not able to be completely removed, standard pharmacotherapy has historically consisted of peptide somatostatin receptor ligands, a GH receptor antagonist, and off-label use of dopamine agonists.

There are three injected somatostatin analogs approved for the treatment of acromegaly: octreotide (marketed by Novartis AG), lanreotide (marketed by Ipsen Biopharmaceuticals, Inc.) and pasireotide (marketed by Recordati Rare Diseases Inc.). Oral octreotide (marketed by Chiesi Farmaceutici) is approved in the U.S. for long-term maintenance treatment in acromegaly patients who have responded to and tolerated treatment with octreotide or lanreotide. Pegvisomant (marketed by Pfizer Inc.) is a daily injectable GHRA and is generally used in patients not fully controlled on somatostatin analogs. Orally administered dopamine agonists, such as bromocriptine and cabergoline, are also used. In December 2021, the FDA approved a biosimilar of lanreotide injection, followed by the approval of a generic lanreotide injection in May 2024 for the treatment of acromegaly, CS, and GEP-NETs. Both products are manufactured by Cipla Ltd. Additionally, in December 2023, the FDA approved an octreotide acetate injectable suspension for treating acromegaly and CS. Other products in clinical development include new formulations of peptide somatostatin agonists (Camurus AB), GH receptor antagonists (Alexion Pharmaceuticals, Inc./AstraZeneca PLC) and anti-GHRA monoclonal antibodies (Marea Therapeutics).

NETs/CS

Long-acting injectable formulations of peptide SSAs are also routinely used in the treatment of NETs to control symptoms associated with hormone hypersecretion and to slow tumor growth in patients with well-differentiated disease. For adults with CS whose symptoms are inadequately controlled by somatostatin therapy alone, telotristat ethyl (marketed by TerSera Therapeutics, Inc.) is available as an orally administered add-on therapy to reduce serotonin-mediated symptoms.

For patients with advanced or metastatic NETs, additional systemic treatment options include peptide receptor radionuclide therapy (PRRT), cytotoxic chemotherapy, and targeted therapies such as mTOR inhibitors and tyrosine kinase inhibitors. However, there is no established consensus regarding optimal treatment sequencing. PRRT is constrained by a limited number of lifetime treatment cycles and is associated with manufacturing, logistical, and administration complexities. Chemotherapy agents lack tumor specificity and generally produce transient responses with cumulative toxicity. Targeted therapies typically provide modest and largely cytostatic clinical benefit, with limited durability of response and the development of treatment resistance during chronic administration.

More recent approvals for the treatment of NETs include FDA approval of Novartis' Lutathera for the treatment of somatostatin receptor-positive GEP-NETs in 2018, and Exelexis' Cabometyx for the treatment of previously treated NETs in 2025. Other companies developing NETs therapeutics that target somatostatin receptors include Oranomed/RadioMedix, ASCIL Biopharm, RayzeBio, Molecular Targeting Technologies Inc., Perspective Therapeutics, and Immunwork Inc. Camurus, Chiesi Farmaceutici, POINT Biopharma Global Inc., RayzeBio, and ITM Isotopen Technologien Munchen are currently engaged in Phase 3 trials of new compounds for use in the treatment of NETs.

CAH

The current treatment algorithm for CAH consists of lifelong daily glucocorticoid supplementation which attempts to address the body's inability to synthesize cortisol as well as its over-production of androgens that results from misregulated steroidogenesis. The inability to precisely dose glucocorticoids can often lead to enduring cycles of over- or under-treatment. Under-treatment can result in adrenal crisis and intramuscular stress doses of glucocorticoid for acute illness are common.

In December 2024, the FDA approved an oral CRF1 receptor antagonist, crinecerfont (marketed by Neurocrine Biosciences) as an adjunctive treatment of classic congenital adrenal hyperplasia. Neurocrine Biosciences is also developing a peptide CRF receptor antagonist for CAH. Other companies developing products for potential use in CAH include Lundbeck Pharmaceuticals, and OMass Therapeutics.

ACTH-Dependent Cushing's Syndrome

As with acromegaly, first-line therapy for Cushing's disease is surgery to remove the pituitary tumor if possible. The use of adrenal enzyme inhibitors (metyrapone, ketoconazole and more recently levoketoconazole which gained FDA approval in December 2021 and is marketed by Xeris Pharmaceuticals) prevent the synthesis of cortisol and can improve symptoms. Mifepristone (marketed by Corcept Therapeutics, Inc.), a glucocorticoid receptor antagonist, is approved for control of hyperglycemia in Cushing's syndrome. A generic form of mifepristone has been approved for the treatment of endogenous Cushing's syndrome. Osilodrostat (marketed by Recordati Rare Diseases Inc.), a cortisol synthesis inhibitor, is approved for the treatment of endogenous Cushing's syndrome. The somatostatin agonist pasireotide is also approved for Cushing's disease. Other companies developing products for potential use in Cushing's disease include Corcept Therapeutics, Inc., Sparrow Pharmaceuticals, and Lundbeck Pharmaceuticals.

Earlier Stage Clinical Programs

There may be other earlier-stage clinical programs that, if approved, would compete with our products. Many of our competitors have substantially greater financial, technical and human resources than we have. Additional mergers and acquisitions in the pharmaceutical industry may result in even more resources being concentrated on our competitors. Competition may increase further as a result of advances made in the commercial applicability of technologies and greater availability of capital for investment in these fields. Our success will be based in part on our ability to build and actively manage a portfolio of drugs that address unmet medical needs and create value in patient therapy.

Our Strategic Collaborations

Radionetics Oncology, Inc.

We formed Radionetics in October 2021, together with other investors. Radionetics aims to develop a deep pipeline of novel, targeted, nonpeptide radiopharmaceuticals for the treatment of a broad range of oncology indications. In connection with the formation of Radionetics, we entered into the Radionetics License, granting Radionetics an exclusive world-wide license to certain targets for the development of radiotherapeutics and related radio-imaging agents. As of December 31, 2025, we had an approximate 25% ownership stake in Radionetics consisting of common and preferred stock.

Sanwa Kagaku Kenkyusho Co., Ltd.

In February 2022, we and SKK entered into the SKK License, pursuant to which we granted SKK an exclusive license to develop and commercialize paltusotine in Japan.
.
On June 14, 2022, we and SKK entered into the SKK Clinical Supply Agreement, whereby we are responsible for manufacturing and supplying certain materials to SKK for specified activities under the SKK License.

Loyal License Agreement

On March 24, 2023, we and Loyal entered into the Loyal License, pursuant to which we granted Loyal an exclusive license to develop and commercialize CRN01941, a somatostatin receptor type 2 agonist, for veterinary use.

Intellectual Property

We actively protect our commercially important proprietary technology by, among other methods, obtaining, maintaining, and defending our patent rights. Issued patents can provide protection for varying periods of time, depending upon the date of filing of the patent application, the date of patent issuance and the legal term of patents in the countries in which they are obtained. In general, patents issued for applications filed in the U.S. can provide exclusionary rights for 20 years from the earliest effective non-provisional filing date. In addition, in certain instances, the term of an issued U.S. patent that covers or claims an FDA approved product can be extended to recapture a portion of the term effectively lost as a result of the FDA regulatory review period, which is called patent term extension. The period of patent term extension in the U.S. cannot be longer than five years and the total patent term, including the extension period, must not exceed 14 years following FDA approval of the product. The term of patents outside of the U.S. varies in accordance with the laws of the foreign jurisdiction, but typically is also 20 years from the earliest effective non-provisional filing date. However, the actual protection afforded by a patent varies on a product-by-product basis, from country-to-country, and depends upon many factors, including the type of patent, the scope of its coverage, the availability of regulatory-related extensions, the availability of legal remedies in a particular country and the validity and enforceability of the patent. Some countries also provide mechanisms to recapture a portion of the patent term lost during regulatory review, similar to patent term extension in the U.S.. The amount of patent term that can be recaptured depends on the laws of the relevant jurisdictions. There is no guarantee that the applicable authorities, including the USPTO in the U.S., will agree with our assessment of whether such extensions should be granted, and if granted, the length of such extensions. For more information regarding the risks related to our intellectual property, see "Risk Factors – Risks related to our intellectual property."

We have filed numerous patent applications covering our internally developed product candidates in the U.S. and in jurisdictions outside of the U.S., resulting in multiple issued patents. We file patent applications geographically broadly, in multiple pharmaceutical markets and in alignment with our commercial strategy. We pursue patent protection for inventions and improvements throughout development, including, when possible, compositions of matter, methods of use, dosage regimens, formulations, crystalline forms (polymorphs), manufacturing processes, and others.

We own multiple issued patents and pending patent applications relating to PALSONIFY (paltusotine). Issued patents claiming the compound paltusotine as composition-of-matter have been obtained in the U.S., Europe, China, Japan, and

Brazil, among other jurisdictions, and are estimated to expire in 2037, not including any available patent term adjustments or extensions. We own issued patents and pending patent applications relating to PALSONIFY (paltusotine) methods of use, dosage regimens, formulations, and crystalline forms (polymorphs), which, when issued, are estimated to expire between 2039 and 2046, not including any available patent term adjustments or extensions.

We own multiple issued patents and pending patent applications relating to our ACTH antagonist product candidate atumelnant. Issued patents claiming the compound atumelnant as composition-of-matter have been obtained in the U.S., China, and Japan, among other jurisdictions, and are estimated to expire in 2039, not including any available patent term adjustments or extensions. We own additional pending patent applications relating to our product candidate atumelnant, its methods of use, dosage regimens, and crystalline forms (polymorphs), which, when issued, are estimated to expire between 2042 and 2046, not including any available patent term adjustments or extensions.

We own one U.S. patent and multiple pending patent applications relating to our NDC platform, including as compositions of matter as well as methods of use and dosage regimens, which expire or are estimated to expire between 2043 and 2046, not including any available patent term adjustments or extensions.

We own a variety of other issued patents and pending patent applications related to various compounds, pharmaceutical compositions and methods of use. The issued patents, and any patents that may issue from the pending patent applications, are estimated to expire between 2036 and 2046, not including any available patent term adjustments or extensions.

We also possess substantial know-how and trade secrets relating to the development and commercialization of our product candidates, including related manufacturing processes and technology, which strengthen and maintain our proprietary position in the field of endocrinology. We own registered trademarks and have pending registration applications protecting our corporate marks and product marks, including PALSONIFY™, in the U.S. and in jurisdictions outside of the U.S., in multiple pharmaceutical markets and in alignment with our commercial strategy. We also plan to rely on data exclusivities and market exclusivities, when available, to provide additional protection for our products.

Certain intellectual property rights, including for our lead programs, have been generated through the use of U.S. government funding provided from our SBIR Grants awarded to us by the National Institute of Diabetes and Digestive and Kidney Diseases of the National Institutes of Health, and are therefore subject to certain federal regulations. As a result, the U.S. government may have certain rights to intellectual property embodied in our current or future product candidates pursuant to the Bayh-Dole Act of 1980.

Manufacturing and Supply

We do not own or operate manufacturing facilities for the production of PALSONIFY or our other product candidates and do not currently plan to develop internal manufacturing operations for commercial products or clinical materials.

We rely on third-party CMOs and suppliers for the manufacture of raw materials, drug substance, and finished drug product used in our preclinical research, clinical trials, and commercial activities, and we expect to continue relying on third-party manufacturers for the commercial supply of our products. We oversee these CMOs through a combination of internal personnel and third-party consultants.

Currently, the drug substance for paltusotine is synthesized in India, undergoes a bioavailability optimization step in Portugal, and is then tableted into finished drug product in the U.S.

Sales, Marketing and Distribution

We are a commercial-stage company following the U.S. regulatory approval and commercial launch of PALSONIFY in the fourth quarter of 2025. We market and sell PALSONIFY in the U.S. through a targeted organization focused on specialty physicians treating rare diseases.

Our product support infrastructure includes medical affairs personnel and commercial teams, including a specialty sales force supported by internal marketing, market access, sales operations, and distribution resources. We distribute PALSONIFY in the U.S. through a third-party distributor and manage sales, marketing, and distribution through a combination of internal resources and third-party relationships.

We may elect in the future to utilize additional strategic partners, distributors, or contract sales organizations to support the commercialization of our product candidates.

For more information regarding the risks related to commercialization, see "Risk Factors – Risks related to commercialization of PALSONIFY and our product candidates."

U.S. Government Regulation

Government authorities in the U.S., at the federal, state and local level, and other countries extensively regulate, among other things, the research, development, testing, manufacture, quality control, approval, labeling, packaging, storage, record-keeping, promotion, advertising, distribution, marketing and export and import of products such as those we are developing. A new drug must be approved by the FDA through the NDA process before it may be legally marketed in the U.S. The process of complying with the extensive regulations and obtaining these approvals and, if approved, the subsequent compliance with applicable federal, state and local statutes and regulations require the expenditure of substantial management and financial resources.

Our business is subject to extensive regulation in the U.S., including the FDA as noted above, and by foreign regulatory authorities, including the EMA. We are required in the U.S. and in the other regions and countries we may intend to commercialize our drug products to obtain approval from regulatory authorities before we manufacture, market and sell our products. If our products obtain regulatory approval, they are subject to U.S. and ex-U.S. regulatory agency authority which may require additional testing and reporting, inspections, or changes to product labeling.

U.S. drug development process

In the U.S., the FDA regulates drugs under the FDCA and its implementing regulations. Failure to comply with the applicable U.S. requirements at any time during the product development process, approval process or after approval may subject an applicant to administrative or judicial sanctions. These sanctions could include the FDA's refusal to approve pending applications, withdrawal of an approval, a clinical hold, warning letters, product recalls, product seizures, total or partial suspension of production or distribution, injunctions, fines, refusals of government contracts, restitution, disgorgement or civil or criminal penalties. Any agency or judicial enforcement action could have a material adverse effect on us.

The process required by the FDA before a drug may be marketed in the U.S. generally involves the following:

- completion of preclinical laboratory tests, animal studies and formulation studies in accordance with good laboratory practice regulations and other applicable regulations;
- submission to the FDA of an IND, which must become effective before human clinical trials may begin;
- performance of adequate and well-controlled human clinical trials in accordance with GCP requirements to establish the safety and efficacy of the proposed drug for its intended use;
- submission to the FDA of an NDA after completion of all pivotal trials;
- satisfactory completion of an FDA pre-approval inspection of the drug product's manufacturing facility or facilities to assess compliance with cGMP requirements; and
- FDA review and approval of the NDA.

Once a product candidate is identified for development, it enters the preclinical testing stage. Preclinical tests include laboratory evaluations of product chemistry, toxicity and formulation, as well as animal studies. The IND automatically becomes effective 30 days after receipt by the FDA, unless the FDA, within the 30-day time period, places the clinical trial on a clinical hold. In such a case, the IND sponsor and the FDA must resolve any outstanding concerns before the clinical trial can begin. Clinical holds also may be imposed by the FDA at any time before or during clinical trials due to safety concerns about on-going or proposed clinical trials or non-compliance with specific FDA requirements, and the trials may not begin or continue until the FDA notifies the sponsor that the hold has been lifted.

Clinical trials involve the administration of the investigational product to healthy volunteers or to patients, under the supervision of qualified principal investigators. Each clinical study at each clinical site must be reviewed and approved by an independent institutional review board, prior to the recruitment of subjects. Numerous requirements apply including, but not limited to, GCP regulations, privacy regulations, and requirements related to the protection of human subjects, such as informed consent.

Clinical trials are typically conducted in three sequential phases, but the phases may overlap, and different trials may be initiated with the same product candidate within the same phase of development in similar or differing patient populations.

- Phase 1 studies may be conducted in a limited number of patients but are usually conducted in healthy volunteer subjects. The product candidate is usually tested for safety and, as appropriate, for absorption, metabolism, distribution, excretion, pharmacodynamics and pharmacokinetics.
- Phase 2 usually involves studies in a larger, but still limited, patient population to evaluate preliminarily the efficacy of the product candidate for specific, targeted indications; to determine dosage tolerance and optimal dosage; and to identify possible short-term adverse effects and safety risks.

- Phase 3 trials are undertaken to further evaluate clinical efficacy of a specific endpoint and to test further for safety within an expanded patient population at geographically dispersed clinical study sites.

Post-approval trials, sometimes referred to as Phase 4 studies, may be conducted after initial marketing approval. These trials are used to gain additional experience from the treatment of patients in the intended therapeutic indication. In certain instances, the FDA may mandate the performance of Phase 4 clinical trials as a condition of approval of an NDA.

U.S. review and approval process

The results of product development, preclinical and other non-clinical studies and clinical trials, along with descriptions of the manufacturing process, analytical tests conducted on the chemistry of the drug, proposed labeling and other relevant information are submitted to the FDA as part of an NDA requesting approval to market the product. The submission of an NDA is subject to the payment of substantial user fees; a waiver of such fees may be obtained under certain limited circumstances.

The FDA conducts a preliminary review of all NDAs within the first 60 days after submission, before accepting them for filing, to determine whether they are sufficiently complete to permit substantive review. The FDA may request additional information rather than accept an NDA for filing. In this event, the NDA must be resubmitted with the additional information. The resubmitted application also is subject to review before the FDA accepts it for filing. Once filed, the FDA reviews an NDA to determine, among other things, whether a product is safe and effective for its intended use and whether its manufacturing is cGMP-compliant to assure and preserve the product's identity, strength, quality and purity. Under the PDUFA, guidelines that are currently in effect, the FDA has a goal of ten months from the date of "filing" of a standard NDA for a new molecular entity to review and act on the submission. This review typically takes twelve months from the date the NDA is submitted to FDA because the FDA has approximately two months to make a "filing" decision after it the application is submitted.

The FDA may refer an application for a novel drug to an advisory committee. An advisory committee is a panel of independent experts, including clinicians and other scientific experts, that reviews, evaluates and provides a recommendation as to whether the application should be approved and under what conditions. The FDA is not bound by the recommendations of an advisory committee, but it considers such recommendations carefully when making decisions. Before approving an NDA, the FDA will inspect the facility or facilities where the product is manufactured. Additionally, before approving an NDA, the FDA may inspect one or more clinical trial sites to assure compliance with GCP requirements.

After the FDA evaluates an NDA and conducts inspections of manufacturing facilities where the investigational product and/or its drug substance will be produced, the FDA may issue an approval letter or a CRL. An approval letter authorizes commercial marketing of the drug with prescribing information for specific indications. A CRL indicates that the review cycle of the application is complete, and the application will not be approved in its present form. A CRL usually describes the specific deficiencies in the NDA identified by the FDA and may require additional clinical data, such as an additional clinical trial or other significant and time-consuming requirements related to clinical trials, nonclinical studies or manufacturing. If a CRL is issued, the sponsor must resubmit the NDA or, addressing all of the deficiencies identified in the letter, or withdraw the application. Even if such data and information are submitted, the FDA may decide that the NDA does not satisfy the criteria for approval.

If a product receives regulatory approval, the approval may be significantly limited to specific diseases and dosages or the indications for use may otherwise be limited, which could restrict the commercial value of the product. In addition, the FDA may require a sponsor to conduct Phase 4 testing, which involves clinical trials designed to further assess a drug's safety and effectiveness after NDA approval, and may require testing and surveillance programs to monitor the safety of approved products which have been commercialized. The FDA may also place other conditions on approval including the requirement for a REMS to assure the safe use of the drug. If the FDA concludes a REMS is needed, the sponsor of the NDA must submit a proposed REMS. The FDA will not approve the NDA without an approved REMS, if required. A REMS could include medication guides, physician communication plans or elements to assure safe use, such as restricted distribution methods, patient registries and other risk minimization tools. Any of these limitations on approval or marketing could restrict the commercial promotion, distribution, prescription or dispensing of products.

In addition, the PREA requires a sponsor to conduct pediatric clinical trials for most drugs, for a new active ingredient, new indication, new dosage form, new dosing regimen or new route of administration. Under PREA, original NDAs and supplements must contain a pediatric assessment unless the sponsor has received a deferral or waiver. The required assessment must evaluate the safety and effectiveness of the product for the claimed indications in all relevant pediatric subpopulations and support dosing and administration for each pediatric subpopulation for which the product is safe and effective. The sponsor or FDA may request a deferral of pediatric clinical trials for some or all of the pediatric subpopulations. A deferral may be granted for several reasons, including a finding that the drug is ready for approval for

use in adults before pediatric clinical trials are complete or that additional safety or effectiveness data needs to be collected before the pediatric clinical trials begin. The FDA must send a non-compliance letter to any sponsor that fails to submit the required assessment, keep a deferral current or fails to submit a request for approval of a pediatric formulation.

Orphan drug designation

Under the Orphan Drug Act, the FDA may grant orphan designation to a drug intended to treat a rare disease or condition, which is a disease or condition that affects fewer than 200,000 individuals in the U.S. or, if it affects more than 200,000 individuals in the U.S., there is no reasonable expectation that the cost of developing and making a drug product available in the U.S. for this type of disease or condition will be recovered from sales of the product. Orphan designation must be requested before submitting an NDA. After the FDA grants orphan designation, the identity of the therapeutic agent and its potential orphan use are disclosed publicly by the FDA. Orphan designation does not convey any advantage in or shorten the duration of the regulatory review and approval process.

If a product that has orphan designation subsequently receives the first FDA approval for the disease or condition for which it has such designation, the product is entitled to orphan product exclusivity, which means that the FDA may not approve any other applications to market the same drug for the same disease or condition for seven years, except in limited circumstances, such as a showing of clinical superiority to the product with orphan exclusivity or inability to manufacture the product in sufficient quantities. The designation of such drug also entitles a party to financial incentives such as opportunities for grant funding towards clinical trial costs, tax advantages and user-fee waivers. However, competitors, may receive approval of different products for the indication for which the orphan product has exclusivity or obtain approval for the same product but for a different indication for which the orphan product has exclusivity. Orphan exclusivity also could block the approval of a competing product for seven years if a competitor obtains approval of the same drug as defined by the FDA or if a product candidate is determined to be contained within the competitor's product for the same disease or condition. In addition, if an orphan designated product receives marketing approval for an indication broader than what is designated, it may not be entitled to orphan exclusivity.

Expedited development and review programs

The FDA has a fast track designation program that is intended to expedite or facilitate the process for reviewing new drug products that meet certain criteria. Specifically, new drugs are eligible for fast track designation if they are intended to treat a serious or life-threatening disease or condition and demonstrate the potential to address unmet medical needs for the disease or condition. The sponsor of a fast track product candidate has opportunities for more frequent interactions with the applicable FDA review team during product development and, once an NDA is submitted, the product candidate may be eligible for priority review. With regard to a fast track product candidate, the FDA may consider for review sections of the NDA on a rolling basis before the complete application is submitted, if the sponsor provides a schedule for the submission of the sections of the NDA, the FDA agrees to accept sections of the NDA and determines that the schedule is acceptable, and the sponsor pays any required user fees upon submission of the first section of the NDA.

A product candidate intended to treat a serious or life-threatening disease or condition may also be eligible for breakthrough therapy designation to expedite its development and review. A product candidate can receive breakthrough therapy designation if preliminary clinical evidence indicates that the product candidate, alone or in combination with one or more other drugs or biologics, may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. The designation includes all of the fast track program features, as well as more intensive FDA interaction and guidance beginning as early as Phase 1 and an organizational commitment to expedite the development and review of the product candidate, including involvement of senior managers.

Any product candidate submitted to the FDA for approval, including a product candidate with a fast track designation or breakthrough designation, may also be eligible for other types of FDA programs intended to expedite development and review, such as priority review and accelerated approval. An NDA is eligible for priority review if the product candidate is designed to treat a serious condition, and if approved, would provide a significant improvement in safety or efficacy compared to marketed products. The FDA will attempt to direct additional resources to the evaluation of an application for a new drug designated for priority review in an effort to facilitate the review. The FDA endeavors to review applications with priority review designations within six months of the filing date as compared to ten months for review of new molecular entity NDAs under its current PDUFA review goals.

In addition, a product candidate may be eligible for accelerated approval. Drug products intended to treat serious or life-threatening diseases or conditions may be eligible for accelerated approval upon a determination that the product candidate has an effect on a surrogate endpoint that is reasonably likely to predict clinical benefit, or on a clinical endpoint that can be measured earlier than irreversible morbidity or mortality, that is reasonably likely to predict an effect on irreversible morbidity or mortality or other clinical benefit, taking into account the severity, rarity, or prevalence of the condition and

the availability or lack of alternative treatments. As a condition of approval, the FDA generally requires that a sponsor of a drug receiving accelerated approval perform adequate and well-controlled confirmatory clinical trials. Drugs receiving accelerated approval may be subject to expedited withdrawal procedures if the sponsor fails to conduct the required confirmatory trials in a timely manner or if such trials fail to verify the predicted clinical benefit. In addition, the FDA currently requires as a condition for accelerated approval pre-approval of promotional materials, which could adversely impact the timing of the commercial launch of the product.

Fast track designation, priority review and breakthrough therapy designation do not change the standards for approval but may expedite the development or approval process. Even if a product candidate qualifies for one or more of these programs, the FDA may later decide that the product no longer meets the conditions for qualification or decide that the time period for FDA review or approval will not be shortened.

Post-approval requirements

Any products manufactured or distributed pursuant to FDA approvals are subject to pervasive and continuing regulation by the FDA, including, among other things, requirements relating to record-keeping, reporting of adverse experiences, periodic reporting, product sampling and distribution, and advertising and promotion of the product. After approval, most changes to the approved product, such as adding new indications, certain manufacturing changes and additional labeling claims, are subject to further FDA review and approval. Drug manufacturers and other entities involved in the manufacture and distribution of approved drugs are required to register their establishments with the FDA and certain state agencies and are subject to periodic unannounced inspections by the FDA and certain state agencies for compliance with cGMP regulations and other laws and regulations. Changes to the manufacturing process are strictly regulated, and, depending on the significance of the change, may require prior FDA approval before being implemented. Accordingly, manufacturers must continue to expend time, money and effort in the area of production and quality control to maintain compliance with cGMP and other aspects of regulatory compliance.

The FDA may withdraw approval if compliance with regulatory requirements and standards is not maintained or if problems occur after the product reaches the market. Later discovery of previously unknown problems with a product, including adverse events of unanticipated severity or frequency, or with manufacturing processes, or failure to comply with regulatory requirements, may result in revisions to the approved labeling to add new safety information; imposition of post-market studies or clinical studies to assess new safety risks; or imposition of distribution restrictions or other restrictions under a REMS program. Other potential consequences include, among other things:

- restrictions on the marketing or manufacturing of the product, complete withdrawal of the product from the market or product recalls;
- fines, warning letters, or untitled letters;
- clinical holds on clinical studies;
- refusal of the FDA to approve pending applications or supplements to approved applications, or suspension or revocation of product approvals;
- product seizure or detention, or refusal to permit the import or export of products;
- consent decrees, corporate integrity agreements, debarment or exclusion from federal healthcare programs;
- mandated modification of promotional materials and labeling and the issuance of corrective information;
- the issuance of safety alerts, Dear Healthcare Provider letters, press releases and other communications containing warnings or other safety information about the product; or
- injunctions or the imposition of civil or criminal penalties.

In addition, the FDA closely regulates the marketing, labeling, advertising and promotion of drug products. A company can make only those claims relating to safety and efficacy, purity and potency that are approved by the FDA and in accordance with the provisions of the approved label. The FDA and other agencies actively enforce the laws and regulations prohibiting the promotion of off-label uses. Failure to comply with these requirements can result in, among other things, adverse publicity, warning letters, corrective advertising and potential civil and criminal penalties. Physicians may prescribe legally available products for uses that are not described in the product's labeling and that differ from those tested by us and approved by the FDA. Such off-label uses are common across medical specialties. Physicians may believe that such off-label uses are the best treatment for many patients in varied circumstances. The FDA does not regulate the behavior of physicians in their choice of treatments. The FDA does, however, restrict manufacturer's communications on the subject of off-label use of their products.

Marketing exclusivity

Market exclusivity provisions under the FDCA can delay the submission or the approval of certain marketing applications. The FDCA provides a five-year period of non-patent data exclusivity within the U.S. to the first applicant to obtain approval of an NDA for a new chemical entity. A drug is a new chemical entity if the FDA has not previously approved any other new drug containing the same pharmaceutical ingredient, or API, which is the molecule or ion responsible for the action of the drug substance. During the exclusivity period, the FDA may not approve or even accept for review an ANDA or an NDA submitted under Section 505(b)(2), or 505(b)(2) NDA, submitted by another company for another drug based on the same API, regardless of whether the drug is intended for the same indication as the original innovative drug or for another indication, where the applicant does not own or have a legal right of reference to all of the data required for approval. However, an application may be submitted after four years if it contains a certification of patent invalidity or non-infringement to one of the patents listed with the FDA by the innovator NDA holder. PALSONIFY is a new chemical entity.

The FDCA alternatively provides three years of marketing exclusivity for an NDA, or supplement to an existing NDA if new clinical investigations, other than bioavailability studies, that were conducted or sponsored by the applicant are deemed by the FDA to be essential to the approval of the application, for example new indications or dosages of an existing drug. This three-year exclusivity covers only the modification for which the drug received approval on the basis of the new clinical investigations and does not prohibit the FDA from approving ANDAs or 505(b)(2) NDAs for drugs containing the API for the original indication or condition of use. Five-year and three-year exclusivity will not delay the submission or approval of a full NDA. However, an applicant submitting a full NDA would be required to conduct or obtain a right of reference to all of the preclinical studies and adequate and well-controlled clinical trials necessary to demonstrate safety and effectiveness.

Pediatric exclusivity is another type of marketing exclusivity available in the U.S. Pediatric exclusivity provides for an additional six months of marketing exclusivity attached to another period of exclusivity if a sponsor conducts clinical trials in children in response to a written request from the FDA. The issuance of a written request does not require the sponsor to undertake the described clinical trials.

U.S. coverage and reimbursement

Significant uncertainty exists as to the coverage and reimbursement status of pharmaceutical products. Patients in the U.S. generally rely on third-party payors to reimburse part or all of the costs associated with their prescription drugs. Sales in the U.S. will depend in part on the coverage and reimbursement levels set by governmental authorities, private health insurers, and other third-party payors. As a threshold for coverage and reimbursement, third-party payors generally require that drug products have been approved for marketing by the FDA. Third-party payors also are increasingly challenging the effectiveness of and prices charged for medical products and services.

The process for determining whether a payor will provide coverage for a product is typically separate from the process for setting the reimbursement rate that the payor will pay for the product. A payor's decision to provide coverage for a product does not imply that an adequate reimbursement rate will be available. No uniform policy for coverage and reimbursement for products exists among third-party payors in the U.S.; therefore, coverage and reimbursement for products can differ significantly from payor to payor. Further, coverage under certain government programs, such as Medicare and Medicaid, may not be available for certain pharmaceutical products. CMS decides whether and to what extent a new product will be covered and reimbursed under Medicare, and private third-party payors often follow CMS's decisions regarding coverage and reimbursement to a substantial degree. However, one third-party payor's determination to provide coverage for a pharmaceutical product does not assure that other payors will also provide coverage for the pharmaceutical product. As a result, the coverage determination process will likely be a time-consuming and costly process, with no assurance that coverage and adequate reimbursement will be applied consistently or obtained in the first instance. Further, coverage policies and third-party reimbursement rates may change at any time.

Third-party payors are increasingly challenging the price and examining the medical necessity and cost-effectiveness of medical products and services, in addition to their safety and efficacy. In order to obtain coverage and reimbursement for any future products that might be approved for marketing, we may need to conduct expensive studies in order to demonstrate the medical necessity and cost-effectiveness of any products, which would be in addition to the costs expended to obtain regulatory approvals. Third-party payors may not consider certain pharmaceutical products to be medically necessary or cost-effective compared to other available therapies, or the rebate percentages required to secure favorable coverage may not yield an adequate margin over cost or may not enable us to maintain price levels sufficient to realize an appropriate return on our investment in drug development. These payors may limit coverage through formulary placement, prior authorization, or other utilization management requirements, and they may reduce payment amounts or refuse to cover our products altogether. Changes in laws, regulations, or payor policies could adversely affect coverage, reimbursement levels, and the commercial success of PALSONIFY and any products we may commercialize in the future.

Healthcare reform

In the U.S. and some foreign jurisdictions, several legislative and regulatory changes and proposed changes have occurred that could prevent or delay marketing approval of drug product candidates, restrict or regulate post-approval activities, and affect the profitable sale of drug product candidates.

In the U.S., the pharmaceutical industry has been significantly affected by major legislative initiatives, including the 2010 Patient Protection and Affordable Care Act, as subsequently amended by the Health Care and Education Reconciliation Act (collectively the "ACA"), which: (1) increased the minimum Medicaid rebates owed by manufacturers under the Medicaid Drug Rebate Program and extended the rebate program to individuals enrolled in Medicaid managed care organizations; (2) established an annual fee on any entity that manufactures or imports certain specified branded prescription drugs and biologic agents; (3) expanded the 340B drug pricing program by adding new entities to the program; (4) created a new Patient-Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research; (5) created a new Medicare Part D coverage gap discount program, in which manufacturers must agree to offer 70% point-of-sale discounts off negotiated prices of applicable brand drugs to eligible beneficiaries during their coverage gap period, as a condition for the manufacturer's outpatient drugs to be covered under Medicare Part D; and (8) established a Center for Medicare and Medicaid Innovation at the CMS to test innovative payment and service delivery models to lower Medicare and Medicaid spending, potentially including prescription drugs.

Since its enactment, there have been many challenges to the ACA. On June 17, 2021, the U.S. Supreme Court dismissed the most recent judicial challenge to the ACA without specifically ruling on the constitutionality of the ACA.

Other legislative changes have been proposed and adopted since the ACA was enacted, including aggregate reductions of Medicare payments to providers. In addition, the American Rescue Plan Act of 2021, which went into effect on January 1, 2024, eliminated the statutory Medicaid drug rebate cap, previously set at 100% of a drug's AMP. Moreover, there has been heightened governmental scrutiny of how manufacturers set prices for their marketed products. Several federal and state legislative efforts were designed to bring more transparency to product pricing and reform government program reimbursement methodologies for drug products. The IRA requires manufacturers of certain drugs to engage in price negotiations with Medicare (beginning in 2026); imposes rebates under Medicare Part B and Medicare Part D to penalize price increases that outpace inflation; and replaces the Part D coverage gap discount program with a new discounting program (which began in 2025). However, because the IRA permits the Department of Health and Human Services (HHS) to implement many of these provisions through guidance, as opposed to regulation, for the initial years, it is currently unclear how the IRA will be effectuated. At the state level, legislatures have increasingly passed legislation and implemented regulations designed to control pharmaceutical product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing.

U.S. healthcare fraud and abuse laws and compliance requirements

Federal and state healthcare laws and regulations govern business practices in the biopharmaceutical industry. These laws include legal authority pertaining to reducing fraud and abuse, increasing transparency, and addressing drug pricing and payments.

The various federal and state laws designed to curb healthcare fraud and abuse include the federal Anti-Kickback Statute, civil and criminal false claims laws, and data privacy and security laws, such as HIPAA. The federal Anti-Kickback Statute prohibits individuals or entities from knowingly and willfully offering, paying, soliciting or receiving any form of remuneration, directly or indirectly, to induce or in return for of the generation of business involving any item or service reimbursable under Medicare, Medicaid or other federal healthcare programs. No actual knowledge or specific intent to violate the statute is necessary in order to have committed a violation.

The civil False Claims Act, prohibits any individual or entity from knowingly presenting, or causing to be presented, a false claim for payment to the federal government or knowingly making, using or causing to be made or used a false record or statement material to a false claim to the federal government. A claim including items or services resulting from a violation of the federal Anti-Kickback Statute can constitute a false claim for purposes of the civil False Claims Act.

HIPAA created additional federal civil and criminal statutes that prohibit knowingly and willfully executing a scheme to defraud any healthcare benefit program. Similar to the federal Anti-Kickback Statute, a person or entity does not need to have actual knowledge or specific intent to violate the statute to commit a violation. Similar state anti-kickback and false claims laws may apply to business practices, including but not limited to, research, distribution, sales and marketing arrangements and claims involving healthcare items or services reimbursed by non-governmental third-party payors, including private insurers, or by patients themselves. Other state laws restrict payments that may be made to healthcare providers and other potential referral sources.

Designed to increase transparency, the federal Physician Payments Sunshine Act requires certain manufacturers of drugs, devices, biologics and medical supplies for which payment is available under Medicare, Medicaid or the Children's Health Insurance Program, to annual report payments and transfers of value to physicians, certain non-physician practitioners, and teaching hospitals, plus physician ownership, to CMS.

Certain state laws also require drug manufacturers to file reports relating to pricing and marketing information which requires tracking gifts and other remuneration and items of value provided to physicians, other healthcare providers and entities, or require the registration of pharmaceutical sales representatives. Other state laws require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government.

Efforts to ensure compliance with applicable healthcare laws and regulations can involve substantial costs. Violations of healthcare laws can result in significant civil, criminal and administrative penalties, including monetary fines, imprisonment, exclusion from participation in federal healthcare programs, integrity oversight and reporting obligations, contractual damages, reputational harm, diminished profits and future earnings, and curtailment or restructuring of operations.

Data Privacy and Security

Numerous state, federal and foreign laws, including consumer protection laws and regulations, govern the collection, dissemination, use, access to, confidentiality and security of personal information, including health-related information. In the U.S., numerous federal and state laws and regulations, including data breach notification laws, health information privacy laws, and consumer protection laws and regulations (e.g., Section 5 of the FTC Act), that govern the collection, use, disclosure, and protection of health-related and other personal information could apply to our operations or the operations of our partners.

For example, California enacted the CCPA effective January 1, 2020, which gives California residents expanded rights to access, correct, and delete their personal information, opt out of certain personal information sharing and disclosure, and receive detailed information about how their personal information is used. The CCPA provides for civil penalties for violations, as well as a private right of action for data breaches that has increased the likelihood of, and risks associated with, data breach litigation. The CCPA may increase our compliance costs and potential liability. Further, the CPRA, generally went into effect on January 1, 2023, and significantly amends the CCPA. The CPRA imposes additional data protection obligations on covered businesses, including additional consumer rights processes, limitations on data uses, new audit requirements for higher risk data, and opt outs for certain uses of sensitive data. It also creates a new California data protection agency authorized to issue substantive regulations and could result in increased privacy and information security enforcement, and additional compliance investment and potential business process changes may be required. Similar laws have passed or been proposed in other states and at the federal level.

In addition, certain foreign laws govern the privacy and security of personal data, including health-related data. Privacy and security laws, regulations, and other obligations are constantly evolving, may conflict with each other to complicate compliance efforts, and can result in investigations, proceedings, or actions that lead to significant civil and/or criminal penalties and restrictions on data processing. See "Risk Factors – Risks related to our business operations and industry" for additional information about the risks to our business associated with a breach or compromise to our information technology systems.

Cybersecurity

In the normal course of business, we may collect and store personal information and certain sensitive company information, including proprietary and confidential business information, trade secrets, intellectual property, information regarding trial participants in connection with clinical trials, sensitive third-party information and employee information. To protect this information, we have implemented a cybersecurity program, described under Item 1C, "Cybersecurity" below. Nonetheless, our security measures cannot guarantee that a significant cyberattack will not occur. A successful attack on our information technology systems could have significant consequences to the business. See "Risk Factors – General Risk Factors" for additional information about the risks to our business associated with a breach or compromise to our information technology systems.

Employees and Human Capital Resources

As of February 13, 2026, we had 594 full-time employees, 150 of whom have a Ph.D. or M.D. None of our employees are represented by labor unions or covered by collective bargaining agreements. We consider our relationship with our employees to be good. In addition, we rely on a number of consultants to assist us.

Our human capital strategy centers on attracting, developing, and retaining top talent to drive organizational success and deliver long-term shareholder value. We achieve this through a holistic approach that combines competitive compensation

offerings with HR best practices. These include robust leadership, management, and individual development opportunities, recognition programs, and engagement activities. Our compensation philosophy complements these programs by offering competitive base pay, equity incentives, and bonuses designed to motivate and reward performance aligned with company objectives.

Insurance

We maintain limited product liability insurance coverage for our clinical trials in the amount of $10 million per occurrence and $10 million in the aggregate. However, insurance coverage is becoming increasingly expensive, and we may not be able to obtain or maintain insurance coverage at a reasonable cost or in sufficient amounts to protect us against losses due to liability.

About Crinetics

We were incorporated in Delaware on November 18, 2008 and commenced operations in 2010.

Our principal executive offices are located at 6055 Lusk Blvd. San Diego, CA 92121, and our telephone number is (858) 450-6464.

Available Information

We make available, free of charge through our website, our annual report on Form 10-K, quarterly reports on Form 10-Q, current reports on Form 8-K, proxy statements, and any amendments to those reports, filed or furnished pursuant to Sections 13(a) or Section 15(d) of the Exchange Act, as soon as reasonably practicable after they have been electronically filed with or furnished to the SEC at www.sec.gov. Our website address is www.crinetics.com. We use our website as a means of disclosing material non-public information and for complying with our disclosure obligations under Regulation FD. Information contained on or accessible through these websites is not incorporated by reference nor otherwise included in this Report, and any references to these websites are intended to be inactive textual references only.

Item 1A. Risk Factors

Investing in our securities involves a high degree of risk. You should consider carefully the risks and uncertainties described below, together with all of the other information included in this Annual Report on Form 10-K, including our consolidated financial statements and the related notes thereto and "Management's Discussion and Analysis of Financial Condition and Results of Operations," before making an investment decision to purchase or sell our securities. If any of the following risks are realized, our business, financial condition, results of operations and prospects could be materially and adversely affected. In that event, the trading price of our securities could decline, and you could lose part or all of your investment. The risks described below are not the only ones that we may face, and additional risks or uncertainties not known to us or that we currently deem immaterial may also impair our business and future prospects.

Risks related to our limited operating history, financial position and capital requirements

We have a limited operating history, have incurred significant operating losses since our inception and expect to continue to incur losses. We may never become profitable or, if we achieve profitability, we may not be able to sustain it.

Pharmaceutical product development is a highly speculative undertaking and involves a substantial degree of risk. We are a pharmaceutical company with a limited operating history upon which you can evaluate our business and prospects. We commenced operations in 2010 and we have focused primarily on organizing and staffing our company, business planning, raising capital, discovering potential product candidates, conducting preclinical studies and clinical trials, and more recently, commercial launch activities for PALSONIFY. While we have obtained FDA regulatory approval and initiated commercial sales of PALSONIFY, we have not yet demonstrated our ability to successfully commercialize the product on a broader or sustained basis.

We are not profitable and have incurred significant operating losses since our inception. Our prospects are highly dependent on the successful launch and commercialization of PALSONIFY and other late stage clinical drug candidates. The commercial success of PALSONIFY will depend on the degree of market acceptance by physicians, patients, health care payors and others in the health care community. To the extent that we cannot generate enough revenue from commercial sales of PALSONIFY, our business, financial condition and results of operations may be materially adversely affected and the price of our securities may decline. Regarding our other late stage clinical drug candidates, if those product candidates are not successfully developed and approved, we may never generate revenue from commercial sales or successfully commercialize those drug candidates. We have incurred cumulative net losses since our inception and, as of December 31, 2025, we had an accumulated deficit of $1.4 billion. Our losses have primarily resulted from expenses incurred in connection with our research and development programs and from selling, general and administrative costs associated with our operations. More recently, we have begun to incur losses associated with pre-commercialization and commercial activities for PALSONIFY associated with its U.S. approval, EMA submission, and pre-commercialization

activities in other jurisdictions. In addition, all of our product candidates will require substantial additional development time and resources before we would be able to apply for or receive regulatory approvals and begin generating revenue from product sales. We expect to continue to incur losses, and we anticipate these losses will increase substantially as we continue our preclinical discovery programs and to develop, seek regulatory approval for PALSONIFY outside of the U.S. and potentially commercialize any other approved products.

To become and remain profitable, we must succeed in developing and commercializing products that generate significant revenue. This will require us to be successful in a range of challenging activities, including completing preclinical studies and clinical trials of our product candidates, discovering additional product candidates, obtaining regulatory approval for our product candidates and manufacturing, marketing and selling any products for which we may obtain regulatory approval. We are in different stages of these activities across the various drug candidates in our pipeline. Other than the FDA approval of PALSONIFY, we have not yet demonstrated an ability to successfully overcome many of the risks and uncertainties frequently encountered by companies in new and rapidly evolving fields, particularly in the biopharmaceutical industry. Because of the numerous risks and uncertainties associated with pharmaceutical product development, commercialization and revenue realization, we are unable to accurately predict the timing or amount of any increased expenses or when, or if, we will be able to achieve profitability. Even if we do achieve profitability, we may not be able to sustain or increase profitability on a quarterly or annual basis. Our failure to become and remain profitable would depress the value of our company and could impair our ability to raise capital, expand our business, maintain our research and development efforts, diversify our product candidates or even continue our operations, any of which could materially and adversely affect our business, prospects, results of operations and the trading price of our common stock.

We will require substantial additional financing to achieve our goals, and a failure to obtain this necessary capital when needed on acceptable terms, or at all, could lead us to delay, limit, reduce, abandon or terminate our product development programs, commercialization efforts or other operations.

The development of biopharmaceutical product candidates and conducting preclinical studies and clinical trials are time-consuming and capital-intensive. We expect our expenses to increase in connection with our ongoing activities, particularly as we continue our commercialization efforts for PALSONIFY and conduct our ongoing and planned clinical trials of paltusotine and atumelnant, continue our research and development activities, conduct preclinical studies for our other development programs, and seek regulatory approval for our current product candidates and any future product candidates, including product candidates that we may develop for NETs and SST2-Expressing Tumors, hyperparathyroidism, polycystic kidney disease, hyperinsulinism, metabolic diseases (including diabetes and obesity) and Graves' Disease (including TED), among other indications. In addition, we expect to incur significant commercialization expenses related to product manufacturing, marketing, sales and distribution of PALSONIFY and, if we obtain regulatory approval, for our other product candidates. Furthermore, we currently incur, and expect to continue to incur, additional costs associated with operating as a public company. Accordingly, we will need to obtain substantial additional funding in connection with our continuing operations. If we are unable to raise capital when needed or on attractive terms, it could lead us to delay, limit, reduce, abandon or terminate some or all of our product candidates, research and development programs, any future commercialization efforts, or other operations.

We believe that our existing cash, cash equivalents and investment securities will enable us to fund our operations for at least the next 12 months. We have based this estimate on assumptions that may prove to be wrong, and we could use our capital resources sooner than we currently expect. Our operating plans and other demands on our cash resources may change as a result of many factors currently unknown to us. Because the outcome of any preclinical study, clinical trial or regulatory review process is highly uncertain, we cannot reasonably estimate the actual amounts necessary to successfully complete the development and commercialization of our product candidates. Our future capital requirements will depend on many factors, including:

- the type, number, scope, progress, results, costs and timing of our preclinical studies and clinical trials of our product candidates which we are pursuing or may choose to pursue in the future;
- our ability to generate revenue through product sales of PALSONIFY and other potential product candidates once approved, if ever, and future licensing arrangements;
- the costs, timing and outcome of regulatory review of our product candidates;
- the costs associated with hiring additional personnel and consultants as our preclinical, clinical and commercial activities increase;
- the costs of and our ability to obtain clinical and commercial supplies for our current product candidates and any other product candidates we may identify and develop;
- the costs and timing of manufacturing for our product candidates, including commercial manufacturing;
- the costs of obtaining, maintaining and enforcing our patents and other intellectual property rights;

- our efforts to enhance operational systems and hire additional personnel to satisfy our obligations as a public company with a commercial pharmaceutical product, including enhanced internal controls over financial reporting, government price reporting and establishing and maintaining an effective compliance program;
- the costs and timing of establishing or securing sales and marketing capabilities for any additional product candidates that are approved;
- our ability to achieve sufficient market acceptance, adequate coverage and reimbursement from third-party payers and adequate market share and revenue for any approved products;
- the terms and timing of establishing and maintaining collaborations, licenses and other similar arrangements;
- costs associated with any products or technologies that we may in-license or acquire;
- the funding of any co-development arrangements we enter into; and
- general economic, industry and market conditions or other events or factors, many of which are beyond our control, such as the impact of any natural disasters, including related to climate change, or public health emergencies, inflation, interest rates, actual or anticipated bank failures, and international military or geopolitical conflicts, including between Russia and Ukraine and in the Middle East.

Accordingly, we may need to seek additional funds sooner than planned, including through public or private equity or debt financings or other sources or through strategic collaborations. In June 2024, we entered into the 2024 Sales Agreement, with the Sales Agents, under which we have and may, from time to time, sell up to $350.0 million of shares of our common stock through the Sales Agents. However, there can be no assurance that the Sales Agents will be successful in consummating future sales based on prevailing market conditions or in the quantities or at the prices that we deem appropriate. In addition, the Sales Agreement may be terminated by us or the Sales Agents at any time upon ten days' notice to the other parties, or by either Sales Agent, with respect to itself, at any time in certain circumstances, including the occurrence of a material adverse change. Attempting to secure additional financing may divert our management from our day-to-day activities, which may adversely affect our ability to commercialize PALSONIFY and develop our other product candidates. Adequate additional financing may not be available to us on acceptable terms, or at all. We do not currently have any active grants nor do we expect grant revenue to be a material source of future revenue. If we are unable to obtain funding on a timely basis, we may be required to significantly curtail, delay or discontinue one or more of our research or development programs, including our clinical trial programs, or any future commercialization of any product candidates, or be unable to sustain or expand our operations or otherwise capitalize on our business opportunities, as desired, any of which could materially affect our business, financial condition and results of operations.

Risks related to the discovery and development and regulatory approval of our product candidates and the commercialization of PALSONIFY

We currently primarily depend on the success of paltusotine, approved as PALSONIFY in the U.S., and have other product candidates in clinical development, and all of our other research programs are still in the preclinical or discovery stage. If we are unable to successfully commercialize PALSONIFY or develop other product candidates or experience significant delays in doing so, our business will be materially harmed.

In September 2025, we obtained FDA approval for PALSONIFY as a once-daily oral treatment in the U.S., to treat adults with acromegaly who had an inadequate response to surgery and/or for whom surgery is not an option. Paltusotine is also being investigated to treat CS associated with neuroendocrine tumors as part of a global, Phase 3 pivotal trial.

With the exception of PALSONIFY, we are still in the development stages for many of our company's assets and other product candidates, such as atumelnant, are in clinical development. All of our other development programs are still in the preclinical or drug discovery stages. We have invested substantial efforts and financial resources in developing our current product candidates, potential product candidates and conducting preclinical studies and clinical trials. Our ability to generate sufficient product revenue for profitability, which may not occur for many years, if ever, will depend heavily on the successful development and eventual commercialization of our product candidates. The successful commercialization of PALSONIFY and of our other product candidates obtaining marketing approval will depend on several factors, including the factors discussed elsewhere in this "Risk Factors" section, and on the completion of each of the following:

- completion of preclinical studies and clinical trials with favorable results;
- acceptance of INDs by the FDA or acceptance of similar regulatory filing by comparable foreign regulatory authorities for the conduct of clinical trials of our product candidates and our proposed design of future clinical trials;
- receipt of marketing approvals from applicable regulatory authorities, including NDAs from the FDA, and maintaining such approvals;
- making arrangements with our third-party manufacturers for, or establishing, commercial manufacturing capabilities;
- maintaining an acceptable safety profile of our products following approval; and

- maintaining and growing an organization of scientists and businesspeople who can develop our products and technology.

If we do not achieve one or more of these factors in a timely manner or at all, we could experience significant delays or an inability to successfully commercialize PALSONIFY or our other product candidates.

The success of our business, including our ability to finance our company and generate any revenue in the future, will primarily depend on the successful commercialization of PALSONIFY, as well as the successful development, regulatory approval and commercialization of our other product candidates, which may never occur. In the future, we may also become dependent on other product candidates that we may develop or acquire. If we are unable to develop, or obtain regulatory approval for, or, if approved, successfully commercialize our product candidates, our business will be materially adversely affected, and we may not be able to generate sufficient revenue to continue our business.

We cannot assure you that we will be able to successfully discover and develop additional product candidates.

The success of our business depends primarily upon our ability to discover, develop, and commercialize products created with our internal capabilities, including the experience of our scientists and drug development staff. We intend to expand our existing pipeline of core assets by advancing lead candidates from current ongoing discovery programs into clinical development. However, research programs to identify potential product candidates are expensive, time-consuming and unpredictable, and can require substantial technical, financial and human resources, whether or not any product candidates are ultimately identified. While we believe we have a highly productive drug discovery and development organization, we may be unsuccessful in discovering additional product candidates, moving such product candidates from preclinical studies into clinical development. Although our product candidates all target endocrine diseases and endocrine-related tumors, we cannot assure you that any additional preclinical programs will be able to progress from candidate identification to Phase 1 clinical proof-of-concept in healthy volunteers. Moreover, any product candidates that we recommend for clinical development may be shown to have harmful side effects or may have other characteristics that may necessitate additional clinical testing or make the product candidates unmarketable or unlikely to receive marketing approval. If any of these events occur, we may choose to or be forced to abandon our discovery or development efforts or a program or programs, which would have a material adverse effect on our business and could potentially cause us to cease operations.

Preclinical and clinical drug development involves a lengthy and expensive process with an uncertain outcome, and the results of preclinical studies and early clinical trials are not necessarily predictive of future results. Our product candidates that we develop may not have favorable results in later clinical trials, if any, or receive regulatory approval, and we may choose to terminate development for strategic reasons.

Preclinical and clinical drug development is expensive and can take many years to complete, and its outcome is inherently uncertain. The historical failure rate for product candidates in our industry is high, and failure can occur at any time during the preclinical study or clinical trial process. Despite promising preclinical or clinical results, any product candidate can unexpectedly fail at any stage of preclinical or clinical development, including termination or abandonment of development for strategic reasons.

The results from preclinical studies or early clinical trials of a product candidate may not predict the results of later clinical trials of the product candidate, and interim, topline or preliminary results of a clinical trial are not necessarily indicative of final results. Product candidates in later stages of clinical trials may fail to show the desired safety and efficacy characteristics despite having progressed through preclinical studies and initial clinical trials or achieving promising early results in earlier studies. It is not uncommon to observe results in clinical trials that are unexpected based on preclinical studies and early clinical trials. Open-label clinical trials are also susceptible to bias that may exaggerate any therapeutic effect or overestimate the risk associated with the product candidate. Furthermore, any safety or efficacy concerns observed in any one of our clinical or non-clinical trials in our targeted indications could limit the prospects for regulatory approval of our product candidates in those and other indications.

For the foregoing reasons, we cannot be certain that our ongoing and planned clinical trials and preclinical studies will be successful, and the failure of any our product candidates could have a material adverse effect on our business, financial condition and results of operations.

Before obtaining marketing approval from regulatory authorities for the sale of our product candidates, we must conduct extensive clinical studies to demonstrate the safety and efficacy of the product candidates in humans. Clinical testing is expensive, time consuming and uncertain as to outcome. We have and in the future may experience delays, a suspension, or the termination of clinical trials at any stage of development and testing of our product candidates, which could result in increased costs to us, delay or limit our ability to generate revenue and adversely affect our commercial prospects. Any clinical trials we undertake may not begin on time, have an effective design, enroll a sufficient number of subjects or be completed on schedule, if at all.

In addition, we have and in the future may rely in part on preclinical, clinical and quality data generated by CROs and other third parties for regulatory submissions for our product candidates, which carry additional risks as discussed below under the section "Risks related to our reliance on third parties." For example, if these third parties do not make data available to us, or, if applicable, do not make regulatory submissions in a timely manner, in each case pursuant to our agreements with them, our development programs may be significantly delayed, and we may need to conduct additional studies or collect additional data independently. In either case, our development costs would increase.

The FDA or comparable foreign regulatory authorities may also require us to conduct additional preclinical studies for any product candidate before they allow us to initiate clinical trials under any IND or similar regulatory filing, which may lead to additional delays and increase the costs of our preclinical development programs.

We do not know whether our planned trials will begin on time or be completed on schedule, if at all. The commencement and completion of clinical trials can be delayed for a number of reasons, including the factors discussed elsewhere in this "Risk Factors" section and any delays, suspensions, or terminations related to:

- the FDA or comparable foreign regulatory authorities disagreeing as to the design or implementation of our clinical studies, or declining to authorize commencing a trial;
- any failure or delay in reaching an agreement with CROs and clinical trial sites, the terms of which can be subject to extensive negotiation and may vary significantly among different CROs and trial sites;
- IRBs, data safety monitoring boards, investigators, or regulators refusing to approve, suspending or terminating the trial at an investigational site, precluding enrollment of additional subjects, or withdrawing their approval of the trial;
- any changes to clinical trial protocol, product candidate formulation, or our manufacturing process that may be necessary or desired, requiring additional preclinical studies or regulatory approval;
- clinical sites deviating from trial protocol or dropping out of a trial;
- manufacturing sufficient quantities of product candidate or obtaining sufficient quantities of combination therapies for use in clinical trials;
- subjects failing to enroll or remain in our trial at the rate we expect, or failing to return for post-treatment follow-ups;
- subjects choosing an alternative treatment for the indication for which we are developing our product candidates, or participating in competing clinical trials;
- lack of adequate funding to continue the clinical trial;
- subjects experiencing severe or unexpected drug-related adverse effects;
- occurrence of serious adverse events in trials of the same class of agents conducted by other companies;
- selection of clinical end points that require prolonged periods of clinical observation or analysis of the resulting data;
- negative or inconclusive results from preclinical testing or clinical trials leading to a decision or requirement to conduct additional preclinical testing or clinical trials or abandon a program;
- a facility manufacturing our product candidates or any of their components being ordered by the FDA or comparable foreign regulatory authorities to temporarily or permanently shut down due to violations of cGMP, regulations or other applicable requirements, or infections or cross-contaminations of product candidates in the manufacturing process;
- third-party clinical investigators losing the licenses or permits necessary to perform our clinical trials, and not performing our clinical trials on our anticipated schedule or consistent with the clinical trial protocol, GCP, or other regulatory requirements;
- third-party contractors not performing data collection or analysis in a timely or accurate manner;
- third-party contractors becoming debarred or suspended or otherwise penalized by the FDA or other government or regulatory authorities for violations of regulatory requirements, in which case we may need to find a substitute contractor, and we may not be able to use some or all of the data produced by such contractors in support of our marketing applications; or
- delays in our clinical trials resulting from external factors including global conflicts or health epidemics.

We could also encounter delays if a clinical trial is suspended or terminated by us or oversight authorities, including the IRBs of the institutions in which such trials are being conducted, the Data Safety Monitoring Board for such trial, or by the FDA or comparable foreign regulatory authorities. Such authorities may impose such a suspension or termination due to a number of factors, including failure to conduct the clinical trial in accordance with regulatory requirements or our clinical protocols, inspection of the clinical trial operations or trial site by the FDA or comparable foreign regulatory authorities resulting in the imposition of a clinical hold, unforeseen safety issues or adverse side effects, failure to demonstrate a benefit from using a drug, changes in governmental regulations or administrative actions or lack of adequate funding to continue the clinical trial. Any such delays in the completion of our ongoing and planned clinical trials for our product

candidates could significantly affect our product development costs, which could have a material adverse effect on our business, financial condition and results of operations. In addition, changes in regulatory requirements and policies may occur, including the imposition of additional regulatory oversight around clinical testing generally or with respect to our product candidates in particular, and we may need to amend clinical trial protocols to comply with these changes. Amendments may require us to resubmit our clinical trial protocols to certain authorities for reexamination, which may impact the costs, timing or successful completion of a clinical trial, and could lead us to delay, reduce, abandon, or terminate development of our product candidates.

Further, conducting clinical trials in foreign countries, as we currently are and may continue to do, for our product candidates presents additional risks that may delay completion of or result in suspension, abandonment or termination of our clinical trials. We must comply with numerous foreign regulatory requirements governing, among other things, the conduct of clinical trials. The foreign regulatory approval process varies among countries, and the time required to obtain approval may differ from that required to obtain FDA approval. Additional risks include the failure of enrolled patients in foreign countries to adhere to clinical protocol as a result of differences in healthcare services or cultural customs, managing additional administrative burdens associated with foreign regulatory schemes, as well as political and economic risks, including war, relevant to such foreign countries.

Moreover, principal investigators for our clinical trials may serve as scientific advisors or consultants to us from time to time and receive cash or equity compensation in connection with such services. Under certain circumstances, we may be required to report some of these relationships to the FDA or comparable foreign regulatory authorities. The FDA or comparable foreign regulatory authority may conclude that a financial relationship between us and a principal investigator has created a conflict of interest or otherwise affected interpretation of the study. The FDA or comparable foreign regulatory authority may therefore question the integrity of the data generated at the applicable clinical trial site and the utility of the clinical trial itself may be jeopardized. This could result in a delay in approval, or rejection, of our marketing applications by the FDA or comparable foreign regulatory authority, as the case may be, and may ultimately lead to the denial of marketing approval of one or more of our product candidates.

In addition, many of the factors that cause, or lead to, termination or suspension of, or a delay in the commencement or completion of, clinical trials may also ultimately lead to the denial of regulatory approval of a product candidate. If we experience delays in the completion of, or termination of, any clinical trial of our product candidates, the commercial prospects of our product candidates will be harmed, and our ability to generate product revenue from any of these product candidates will be delayed. Any delays to our clinical trials could shorten any period during which we may have the exclusive right to commercialize our product candidates and our competitors may be able to bring products to market before we do, and the commercial viability of our product candidates could be significantly reduced. Moreover, any delays in completing our clinical trials will increase our costs, slow down our product candidate development and approval process and jeopardize our ability to commence product sales and generate revenue. We may delay, suspend, abandon or terminate development of our product candidates, or one or more product candidate indications or territories for various strategic reasons. Any of these occurrences may have a material adverse effect on our business, financial condition and prospects.

We may find it difficult to enroll and retain patients in our clinical trials given the limited number of patients who have the diseases for which our product candidates are being developed. If we encounter difficulties enrolling subjects in our clinical trials, our clinical development activities could be delayed or otherwise adversely affected.

We may not be able to initiate or continue clinical trials if we are unable to identify and enroll a sufficient number of eligible subjects to participate in the clinical trials required by the FDA or comparable foreign regulatory authorities. Even once enrolled, we may be unable to retain a sufficient number of patients to complete any of our trials. This process of finding and enrolling subjects may prove costly and is a significant factor in the timing of clinical trials. Patient enrollment and retention is affected by many factors, including the size and nature of the patient population, the proximity of patients to clinical sites, the eligibility and exclusion criteria for the trial, the design of the clinical trial, the risk that enrolled patients will not complete a clinical trial, our ability to obtain and maintain patient consents, including any additional consents necessary for enrollment of adolescent patients, our ability to recruit clinical trial investigators with the appropriate competencies and experience, competing clinical trials and clinicians' and patients' perceptions as to the potential advantages and risks of the product candidate being studied in relation to other available therapies, including any new drugs that may be approved for the indications we are investigating as well as any drugs under development. Potential subjects for any planned or ongoing clinical trials may not be adequately diagnosed or identified with the diseases which we are targeting, and we may encounter difficulties in identifying and enrolling subjects with a stage of disease appropriate for our planned or ongoing clinical trials. Furthermore, any negative results or new safety signals we may report in clinical trials of our product candidates may make it difficult or impossible to recruit and retain patients in other clinical trials we are conducting. Similarly, results reported by our competitors about their product candidates may negatively affect patient recruitment in our clinical trials. Additionally, the FDA or comparable foreign regulatory authorities may modify or

enhance trial requirements, which may affect enrollment. For example, in August 2023, the FDA published a guidance document, "Informed Consent, Guidance for IRBs, Clinical Investigators, and Sponsors," which supersedes past guidance and finalizes draft guidance on informed consent. The FDA's new guidance presents evolving requirements for informed consent which may affect recruitment and retention of patients in clinical trials. Effects on recruitment and retention of patients may hinder or delay a clinical trial and could cause a significant setback to an applicable program.

We may also find it difficult to enroll patients in our clinical trials because some of the conditions for which we currently plan to evaluate our product candidates are orphan or rare diseases with limited patient pools from which to draw for clinical trials. For example, some of our target indications are orphan indications, and in particular, our product candidate, atumelnant, targets CAH, an orphan indication which currently affects approximately 17,000 people in the U.S. The eligibility criteria of our clinical trials will further limit the pool of available trial participants. If eligible patients are unwilling to participate in our trials for any reason, including the existence of concurrent clinical trials for similar patient populations, if they are unwilling to enroll in a clinical trial with a placebo-controlled design or the availability of approved therapies, or we otherwise have difficulty enrolling a sufficient number of patients, the timeline for recruiting subjects, conducting studies and obtaining regulatory approval of our product candidates may be delayed. Our inability to enroll a sufficient number of subjects for any of our current or future clinical trials would result in significant delays beyond our expected timelines, may require us to abandon one or more clinical trials altogether, may result in increased development costs for our product candidates, which could cause the value of our common stock to decline and limit our ability to obtain additional financing.

We cannot assure you that our assumptions used in determining expected clinical trial timelines are correct or that we will not experience delays in enrollment, which would result in the delay of completion of such trials beyond our expected timelines, and result in a material adverse effect on our business, prospects, financial condition and results of operations.

Use of our products and product candidates could be associated with side effects or adverse events during their development or commercialization, which could severely harm our business, reputation, prospects, operating results and financial condition.

As is the case with pharmaceuticals generally, it is likely that there may be side effects and adverse events associated with the use of our product candidates. Results of our clinical trials could reveal a high and unacceptable severity and prevalence of side effects or unexpected characteristics. Undesirable side effects caused by our product candidates, or even by other companies' similar approved drugs or product candidates, could cause us or regulatory authorities to interrupt, delay or halt clinical trials and could result in a more restrictive label or the delay or denial of regulatory approval by the FDA or comparable foreign regulatory authorities. The drug-related side effects could affect patient recruitment or the ability of enrolled patients to complete the trial or result in potential product liability claims. Additionally, the inclusion of critically ill patients in our clinical trials may result in deaths or other adverse medical events due to other therapies or medications that such patients may be using or due to the gravity of such patients' illnesses. Any of these occurrences may harm our business, financial condition and prospects significantly.

Moreover, if our product candidates are associated with undesirable side effects in clinical trials or have characteristics that are unexpected, we may elect to abandon their development or limit their development to more narrow uses or subpopulations in which the undesirable side effects or other characteristics are less prevalent, less severe or more acceptable from a risk-benefit perspective, which may limit the commercial expectations for the product candidate if approved. We may also be required to modify our study plans based on findings in our clinical trials. Many compounds that initially showed promise in early-stage testing have later been found to cause side effects that prevented further development of the compound. In addition, regulatory authorities may draw different conclusions or require additional testing to confirm these determinations.

Further, we have no control over the clinical trials or development program of third parties developing investigational products directed to the same target as one of our programs. Adverse findings or results from any of their clinical trials could adversely affect the commercial prospects of our investigational products and cause our stock price to fluctuate or decline.

It is possible that as we test our product candidates in larger, longer and more extensive clinical trials, including with different dosing regimens and formulations, or as the use of these product candidates becomes more widespread if they receive regulatory approval, illnesses, injuries, discomforts and other adverse events that were observed in earlier trials, as well as conditions that did not occur or went undetected in previous trials, will be reported by subjects. If such side effects become known later in development or upon approval, if any, such findings may harm our business, financial condition and prospects significantly.

In addition, if PALSONIFY or if more of our product candidates receives marketing approval, and we or others later identify undesirable side effects or adverse events caused by such products, a number of potentially significant negative consequences could result, including:

- regulatory authorities may withdraw approvals of such product or require additional warnings on the label, such as a "black box" warning or a contraindication;
- we may be required to limit marketing to narrower uses or subpopulations in which the undesirable side effects, adverse events, or other characteristics are less prevalent, less severe or more acceptable from a risk-benefit perspective;
- we may be required to recall a product or change the way such product is administered to patients;
- we may be required to implement a risk mitigation strategy or limit distribution of a product;
- we could be sued and held liable for harm caused to patients;
- the product could become less competitive; and
- our reputation may suffer.

Any of these events could prevent us from achieving or maintaining market acceptance of the particular product candidate, if approved, and could have a material adverse effect on our business, results of operations and prospects.

Our product candidates are subject to extensive regulation and compliance, which is costly and time consuming and which may cause unanticipated delays or prevent the receipt of the required approvals to commercialize our product candidates.

The research, clinical development, testing, quality control, safety, effectiveness, manufacturing, labeling, packaging, storage, record-keeping, advertising, promotion, marketing, import, export, distribution, post-approval monitoring, and post-approval reporting of our product candidates are subject to extensive regulation by the FDA in the U.S. and by comparable foreign regulatory authorities in foreign markets. In the U.S. and other jurisdictions, neither we nor any future collaborators are permitted to market our product candidates until we receive regulatory approval from the FDA or applicable regulatory authority. The process of obtaining regulatory approval is expensive, often takes many years following the commencement of clinical trials and can vary substantially based upon the type, complexity and novelty of the product candidates involved, as well as the target indications and patient population. Approval policies or regulations may change, new relevant statutes or regulations may be enacted, and the FDA and comparable foreign regulatory authorities have substantial discretion in the drug approval process, including the ability to delay, limit or deny approval of a product candidate for many reasons. Despite the time and expense invested in clinical development of product candidates, regulatory approval is never guaranteed.

Prior to obtaining approval to commercialize a product candidate in the U.S. or abroad, we or our potential future collaborators must demonstrate with substantial evidence from adequate and well-controlled clinical trials, and to the satisfaction of the FDA or comparable foreign regulatory authorities, that such product candidates are safe and effective for their intended uses. Results from nonclinical studies and clinical trials can be interpreted in different ways. Even if we believe the nonclinical or clinical data for our product candidates are promising, such data may not be sufficient to support approval by the FDA and comparable foreign regulatory authorities, which could require us to delay or abandon clinical development plans. Further, requirements regarding clinical trial data may evolve. For example, the FDA published a draft guidance, E6 (R3) Good Clinical Practice, in June 2023, and Annex 2 thereto in December 2024, which seeks to unify standards for clinical trial data for ICH member countries and regions. Changes to data requirements by the FDA or comparable foreign regulatory authorities, as the case may be, may cause the applicable regulatory authorities to require us to conduct additional preclinical studies or clinical trials for our product candidates either prior to or post-approval, or may object to elements of our clinical development program.

The FDA or comparable foreign regulatory authorities can delay, limit or deny approval of a product candidate for many reasons, including:

- such authorities may disagree with the design or implementation of our clinical trials;
- negative or ambiguous results from our clinical trials or results may not meet the level of statistical significance required by the FDA or comparable foreign regulatory agencies for approval;
- serious and unexpected drug-related side effects may be experienced by participants in our clinical trials or by individuals using drugs similar to our product candidates;
- the population studied in the clinical trial may not be sufficiently broad or representative to assure safety in the full population for which we seek approval;
- such authorities may not accept clinical data from trials which are conducted at clinical facilities or in countries where the standard of care is potentially different from that of the U.S.;
- we may be unable to demonstrate that a product candidate's clinical and other benefits outweigh its safety risks;

- such authorities may disagree with our interpretation of data from preclinical studies or clinical trials; such authorities may not agree that the data collected from clinical trials of our product candidates are acceptable or sufficient to support the submission of an NDA or other submission or to obtain regulatory approval in the U.S. or elsewhere, and such authorities may impose requirements for additional preclinical studies or clinical trials;
- such authorities may disagree regarding the formulation, labeling and/or the specifications of our product candidates;
- approval may be granted only for indications that are significantly more limited than what we apply for and/or with other significant restrictions on distribution and use;
- such authorities may find deficiencies in the manufacturing processes or facilities of our third-party manufacturers with which we or any of our potential future collaborators contract for clinical and commercial supplies;
- the approval policies or regulations of such authorities may significantly change in a manner rendering our or any of our potential future collaborators' clinical data insufficient for approval; or
- the FDA or other comparable foreign regulatory authorities may experience disruptions to the review or approval process.

With respect to foreign markets, approval procedures vary among countries and, in addition to the foregoing risks, may involve additional product testing, administrative review periods and agreements with pricing authorities. In addition, events raising questions about the safety of certain marketed pharmaceuticals may result in increased cautiousness by the FDA and comparable foreign regulatory authorities in reviewing new drugs based on safety, efficacy or other regulatory considerations and may result in significant delays in obtaining regulatory approvals. Any delay in obtaining, or inability to obtain, applicable regulatory approvals would prevent us or any of our potential future collaborators from commercializing our product candidates.

Of the large number of drugs in development, only a small percentage successfully complete the FDA or foreign regulatory approval processes and are commercialized. The lengthy approval process as well as the unpredictability of future clinical trial results may result in our failing to obtain regulatory approval to market our product candidates, which would significantly harm our business, financial condition, results of operations and prospects.

Even if we complete clinical trials and receive approval of an NDA or foreign marketing application for our product candidates currently in development, the FDA or comparable foreign regulatory authority may grant approval contingent on the performance of costly additional clinical trials, including Phase 4 clinical trials or the implementation of a REMS, which may be required to ensure safe use of the drug after approval. The FDA or the comparable foreign regulatory authority also may approve a product candidate for a more limited indication or patient population than we originally requested, and the FDA or comparable foreign regulatory authority may not approve the labeling that we believe is necessary or desirable for the successful commercialization of a product. These additional limitations could adversely affect our ability to generate revenue from sales of those products and could materially adversely impact our business and prospects.

Because we have limited financial and managerial resources, we focus on specific product candidates, indications and discovery programs. We may expend our limited resources to pursue a particular product candidate, and as a result, we may abandon, terminate, forgo or delay pursuit of opportunities with other product candidates or in other indications and territories that could have had greater commercial potential. Our resource allocation decisions may cause us to fail to capitalize on viable commercial products or profitable market opportunities. Our spending on current and future research and development programs and product candidates for specific indications may not yield any commercially viable products. If we do not accurately evaluate the commercial potential or target market for a particular product candidate, we may relinquish valuable rights to that product candidate through future collaborations, licenses and other similar arrangements in cases in which it would have been more advantageous for us to retain sole development and commercialization rights to such product candidate.

The FDA's and other regulatory authorities' policies may change, and additional government regulations may be enacted that could prevent, limit or delay regulatory approval of our product candidates. We also cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative action, either in the U.S. or abroad. For example, the prior presidential administrations have taken several executive actions that imposed significant burdens on, or otherwise materially delayed, the FDA's ability to engage in routine oversight activities, such as implementing statutes through rulemaking, issuance of guidance, and review and approval of marketing applications. It is difficult to predict whether or how any current executive orders will be rescinded and replaced under the current administration. The policies and priorities of any administration and the U.S. Congress are unknown and could materially impact the regulations governing our product candidates. If we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we or they are not able to maintain regulatory compliance, we or they may be subject to enforcement action, and we may not achieve or sustain profitability.

We have obtained orphan drug designation from the FDA for paltusotine for the treatment of acromegaly. We also plan to seek orphan drug designations for certain of our other product candidates. However, we may not be able to obtain or maintain orphan drug designations for paltusotine or any of our other product candidates, and we may be unable to maintain the benefits associated with orphan drug designation, including the potential for market exclusivity.

Regulatory authorities in some jurisdictions, including the U.S. and Europe, may designate drugs for relatively small patient populations as orphan drugs. Under the Orphan Drug Act of 1983, the FDA may designate a product as an orphan product if it is intended to treat a rare disease or condition, which is generally defined as a patient population of fewer than 200,000 individuals in the U.S., or a patient population of greater than 200,000 individuals in the U.S., but for which there is no reasonable expectation that the cost of developing the drug will be recovered from sales in the U.S. In the European Union, the EMA's Committee for Orphan Medicinal Products grants orphan drug designation to promote the development of products that are intended for the diagnosis, prevention or treatment of a life-threatening or chronically debilitating condition affecting not more than five in 10,000 persons in the European Union. We have obtained orphan drug designation for paltusotine in the U.S. for the treatment of acromegaly, and we may seek similar orphan drug designations in other territories. We may also seek orphan drug designations for certain of our other product candidates.

There can be no assurance, however, that the FDA or the EMA's Committee for Orphan Medicinal Products will grant orphan designation for any indication for which we apply. Even if we do receive such designations, we do not know if, when, or how the FDA or the EMA may change the orphan drug regulations and policies in the future. The FDA and Congress may further reevaluate the Orphan Drug Act and its regulations and policies. This may be particularly true in light of a decision from the Court of Appeals for the 11th Circuit in September 2021 finding that, for the purpose of determining the scope of exclusivity, the term "same disease or condition" means the designated "rare disease or condition" and could not be interpreted by the FDA to mean the "indication or use." Although there have been legislative proposals to overrule this decision, they have not been enacted into law. On January 23, 2023, the FDA announced that, in matters beyond the scope of that court order, the FDA will continue to apply its existing regulations tying orphan-drug exclusivity to the uses or indications for which the orphan drug was approved. We do not know if, when, or how the FDA or Congress may change the orphan drug regulations and policies in the future, and it is uncertain how any changes might affect our business. Depending on what changes the FDA may make to its orphan drug regulations and policies, our business could be adversely impacted. Additionally, on April 26, 2023, the European Commission adopted a proposal for a new Directive and a new Regulation, and in April 2024, the European Parliament adopted its position on the proposal. If made into law, this proposal will revise and replace the existing general pharmaceutical legislation and may make it more difficult to obtain orphan designation in from the EMA and reduce baseline exclusivity periods.

In the U.S., orphan designation entitles a party to financial incentives such as opportunities for grant funding towards clinical trial costs, tax advantages and user-fee waivers. Despite this designation, we may be unable to maintain the benefits associated with orphan drug status, including market exclusivity. In addition, if a product candidate that has orphan designation subsequently receives the first FDA approval for the disease for which it has such designation, the product is entitled to orphan drug exclusivity, which means that the FDA may not approve any other applications, including an NDA, to market the same drug for the same disease or condition for seven years, except in limited circumstances, such as a showing of clinical superiority to the product with orphan drug exclusivity or where the manufacturer is unable to assure sufficient product quantity. The applicable exclusivity period is ten years in Europe, but such exclusivity period can be reduced to six years if a product no longer meets the criteria for orphan designation or if the product is sufficiently profitable so that market exclusivity is no longer justified.

Even if we obtain orphan drug exclusivity for a product, that exclusivity may not effectively protect the product from competition because different drugs can be approved for the same condition. Even after an orphan drug is approved, the FDA or comparable foreign regulatory authority can subsequently approve the same drug for the same condition if such regulatory authority concludes that the later drug is clinically superior if it is shown to be safer, more effective or makes a major contribution to patient care. Orphan drug designation neither shortens the development time or regulatory review time of a drug nor gives the drug any advantage in the regulatory review or approval process.

We have conducted, and continue to conduct, clinical trials for our current product candidates outside of the U.S., and we may do so for our other product candidates. However, conducting trials outside of the U.S. exposes us to additional risks, which could materially harm our business.

We are conducting, and may in the future conduct, certain of our clinical trials at centers outside of the U.S. The acceptance of study data from clinical trials conducted outside the U.S. or another jurisdiction by the FDA or a comparable foreign regulatory authority may be subject to certain conditions or may not be accepted at all. For example, in cases where data from foreign clinical trials are intended to serve as the sole basis for marketing approval in the U.S., the FDA will generally not approve the application on the basis of foreign data alone unless (i) the data are applicable to the U.S. population and U.S. medical practice; (ii) the trials were performed by clinical investigators of recognized competence and

pursuant to GCP regulations; and (iii) the data may be considered valid without the need for an on-site inspection by the FDA, or if the FDA considers such inspection to be necessary, the FDA is able to validate the data through an on-site inspection or other appropriate means. In addition, even where the foreign study data are not intended to serve as the sole basis for approval, the FDA will not accept the data as support for an application for marketing approval unless the study is well-designed and well-conducted in accordance with GCP requirements and the FDA is able to validate the data from the study through an onsite inspection if deemed necessary. Many foreign regulatory authorities have similar approval requirements. In addition, such foreign trials would be subject to the applicable local laws of the foreign jurisdictions where the trials are conducted. If the FDA, U.K. MHRA or other foreign equivalents do not accept any data generated from other jurisdictions, we would likely be required to conduct additional clinical trials, which would be costly and time consuming, and delay aspects of our development plan, which could harm our business.

Conducting trials outside the U.S. also exposes us to additional risks, including risks associated with:

- additional foreign regulatory requirements;
- foreign exchange fluctuations;
- compliance with foreign manufacturing, customs, shipment and storage requirements;
- cultural differences in medical practice and clinical research;
- diminished protection of intellectual property in some countries; and
- interruptions or delays in our trials resulting from geopolitical events, such as war or terrorism.

In addition, as a result of Brexit, the United Kingdom operates under a distinct regulatory regime from the European Union, and while current United Kingdom rules on clinical trials are derived from prior European Union legislation (as implemented into United Kingdom law), United Kingdom rules may continue to diverge from European Union laws. For example, the EU CTR provides for a streamlined clinical trial application and assessment procedure covering multiple EU Member States. However, this has not been implemented into United Kingdom law, and a separate application must be submitted for clinical trial authorization in the United Kingdom. In addition, Great Britain is not covered by the centralized procedure for obtaining EEA-wide marketing authorizations from the EMA for medicinal products and a separate process for authorization of drug products is required in Great Britain. Until December 31, 2023, the U.K.'s MHRA could rely on a decision taken by the European Commission on the approval of a new marketing authorization in the centralized procedure, in order to more quickly grant a new Great Britain marketing authorization, however a separate application was still required. Since January 1, 2024, the IRP is a new international recognition framework in the U.K. that replaces the European Commission Decision Reliance Procedure, whereby the MHRA gives regard to decisions made by certain foreign regulators, including the EMA and the competent authorities of the EU Member States. Under this procedure, the MHRA takes into account the decision-making of such foreign regulators and conducts a targeted assessment of the applications submitted through the IRP, but retains the authority to reject applications if the evidence provided is considered insufficiently robust. Additionally, rules apply to the import of investigational medicinal products from the European Union and European Economic Area to the United Kingdom. As a result, there may be additional administrative burdens including disruptions to and uncertainty surrounding our planned clinical trials and activities in the United Kingdom and the European Union, impacting relationships with our existing and prospective customers, partners, vendors and employees. Although the EU-UK Trade and Cooperation Agreement, which became effective in January 1, 2021, includes zero tariffs on goods and provides for regulatory cooperation, the agreement does not cover all regulatory areas regarding supply of medicinal products, which will likely be subject to ongoing bilateral discussions, which could further change the relationship between the United Kingdom and the European Union in this regard. Any delay in obtaining, or an inability to obtain, any regulatory approvals, as a result of Brexit or otherwise, would delay or prevent us from commercializing our current or future product candidates in the U.K. and could restrict our ability to generate revenue from that market. Changes impacting our ability to conduct business in the United Kingdom or other European Union countries, or changes to the regulatory regime applicable to our operations in those countries (such as with respect to the approval of our product candidates), may have a material adverse impact on our business, financial condition and prospects.

Changes in U.S. and international trade policies, particularly with respect to China, Europe and India may adversely impact our business and operating results.

The U.S. government has recently made statements and taken certain actions that may lead to potential changes to U.S. and international trade policies, including imposing several rounds of tariffs and export control restrictions affecting certain products manufactured in China. Both China and the U.S. have each imposed tariffs indicating the potential for further trade barriers, including the U.S. Commerce Department adding numerous Chinese entities to its "unverified list," which requires U.S. exporters to go through more procedures before exporting goods to such entities. Further, the current administration has imposed tariffs on foreign imports into the U.S., signaled intent to negotiate and enter into a variety of new trade agreements that could cause disruptions or unexpected costs associated with importation and any potential , reciprocal tariffs. As of February 2026, the US and India agreed to a reciprocal tariff rate of 18 percent on goods imported from India. It is unknown whether and to what extent new tariffs, export controls, or other new laws or regulations will be

adopted, or the effect that any such actions would have on us or our industry. Any unfavorable government policies on international trade, such as export controls, capital controls or tariffs, may increase the cost of manufacturing our product candidates and platform materials, affect our ability to commercialize our product candidates if approved, the competitive position of our product candidates, and import or export of raw materials and finished product candidate used in our preclinical studies and clinical trials, particularly with respect to any product candidates and materials that we import from China. If any new tariffs, export controls, legislation and/or regulations are implemented, or if existing trade agreements are renegotiated or, in particular, if either the U.S. or Chinese government takes retaliatory trade actions due to the recent trade tension, such changes could have an adverse effect on our business, financial condition and results of operations.

Initial, interim, topline and preliminary data from our clinical trials that we announce or publish from time to time may change as more patient data becomes available and is subject to audit and verification procedures that could result in material changes in the final data.

From time to time, we may publicly disclose initial, interim, preliminary or topline or data from our clinical studies, which is based on a preliminary analysis of then-available data, and the results and related findings and conclusions are subject to change following a more comprehensive review of the data related to the particular study or trial. We also make assumptions, estimations, calculations and conclusions as part of our analyses of data, and we may not have received or had the opportunity to fully and carefully evaluate all data. As a result, the initial, topline or other preliminary results that we report may differ from future results of the same studies, or different conclusions or considerations may qualify such results, once additional data have been received and fully evaluated. Preliminary and topline data also remain subject to audit and verification procedures that may result in the final data being materially different from the preliminary data we previously published. As a result, interim, topline or other preliminary data should be viewed with caution until the final data are available. From time to time, we may also disclose initial or interim data from our clinical studies. Initial and interim data from clinical trials that we may complete are subject to the risk that one or more of the clinical outcomes may materially change as patient enrollment continues and more patient data become available. Adverse differences between initial, preliminary, topline or interim data and final data could significantly harm our business prospects.

Moreover, preclinical and clinical data are often susceptible to varying interpretations and analyses. Others, including regulatory agencies, may not accept or agree with our assumptions, estimates, calculations, conclusions or analyses or may interpret or weigh the importance of data differently, which could impact the value of the particular program, the approvability or commercialization of the particular product candidate or product and our company in general. In addition, the information we choose to publicly disclose regarding a particular study or clinical trial is based on what is typically extensive information, and you or others may not agree with what we determine is the material or otherwise appropriate information to include in our disclosure, and any information we determine not to disclose may ultimately be deemed significant with respect to future decisions, conclusions, views, activities or otherwise regarding a particular drug, drug candidate or our business. If the interim, preliminary, or topline data that we report differ from actual results, or if others, including regulatory authorities, disagree with the conclusions reached, our ability to obtain approval for, and commercialize, our product candidates may be harmed, which could harm our business, operating results, prospects or financial condition.

Risks related to commercialization of PALSONIFY and our product candidates

We are subject to ongoing regulatory obligations and continued regulatory review, which may result in significant additional expense. Additionally, PALSONIFY and, if approved, our other product candidates could be subject to labeling and other restrictions on marketing or withdrawal from the market, and we may be subject to penalties if we fail to comply with regulatory requirements or if we experience unanticipated problems.

The FDA or comparable foreign regulatory authorities may impose significant restrictions on a product's indicated uses or marketing or impose ongoing requirements for potentially costly and time-consuming post-approval studies, post-market surveillance or clinical trials to monitor the safety and efficacy of the product. For example, the FDA may also require the implementation of a REMS as a condition of approval of our product candidates, which could include requirements for a medication guide, physician communication plans or additional elements to ensure safe use, such as restricted distribution methods, patient registries and other risk minimization tools. In addition, the manufacturing processes, labeling, packaging, distribution, adverse event reporting, storage, advertising, promotion, import, export and recordkeeping for our products are subject to extensive and ongoing regulatory requirements. These requirements include submissions of safety and other post-marketing information and reports, registration, as well as continued compliance with cGMPs and GCP requirements for any clinical trials that we conduct post-approval.

In addition, the FDA strictly regulates the promotional claims that may be made about drug products. In particular, a product may not be promoted for uses that are not approved by the FDA as reflected in the product's approved labeling, but physicians may nevertheless prescribe it to their patients in a manner that is inconsistent with the approved label. If we are found to have promoted such off label uses, we may become subject to significant liability. The FDA and other agencies

actively enforce the laws and regulations prohibiting the promotion of off-label uses, and a company that is found to have improperly promoted off-label uses may be subject to significant sanctions. The federal government has levied large civil and criminal fines against companies for alleged improper promotion and has enjoined several companies from engaging in off-label promotion. The FDA has also requested that companies enter into consent decrees or permanent injunctions under which specified promotional conduct is changed or curtailed.

Furthermore, later discovery of previously unknown problems with our products, including adverse events of unanticipated severity or frequency, or with our third-party manufacturers or manufacturing processes, or failure to comply with regulatory requirements, may result in, among other things:

- restrictions on the marketing or manufacturing of our products, withdrawal of the product from the market or voluntary or mandatory product recalls;
- restrictions on product distribution or use, or requirements to conduct post-marketing studies or clinical trials;
- fines, restitutions, disgorgement of profits or revenue, warning letters, untitled letters or holds on clinical trials;
- refusal by the FDA or comparable foreign regulatory authorities to approve pending applications or supplements to approved applications filed by us or suspension or revocation of approvals;
- product seizure or detention, or refusal to permit the import or export of our products; and
- injunctions or the imposition of civil or criminal penalties.

The occurrence of any event or penalty described above may inhibit our ability to commercialize PALSONIFY and our other product candidates and generate revenue and could require us to expend significant time and resources in response and could generate negative publicity.

We also cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative or executive action, either in the U.S. or abroad. The FDA's and other regulatory authorities' policies may change, and additional government regulations may be enacted that could prevent, limit or delay commercialization of PALSONIFY and our other product candidates. For example, prior presidential administrations have taken several executive actions that imposed significant burdens on, or otherwise materially delayed, the FDA's ability to engage in routine oversight activities, such as implementing statutes through rulemaking, issuance of guidance, and review and approval of marketing applications. It is difficult to predict whether or how any current orders will be rescinded and replaced under the current administration. The policies and priorities of any administration and the U.S. Congress are unknown and could materially impact the regulations governing our product candidates. If we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we are not able to maintain regulatory compliance, we may be subject to enforcement action, as a result of which we may not achieve or sustain profitability, which would have a material adverse effect on our business, reputation, prospectus and financial condition.

Disruptions at the FDA and other government agencies could hinder their ability to hire, retain or deploy key leadership and other personnel, or otherwise prevent new or modified products from being developed, approved, or commercialized in a timely manner or at all, which could negatively impact our business.

The ability of the FDA and other government agencies to review and approve new products can be affected by a variety of factors, including government budget and funding levels, statutory, regulatory and policy changes, staffing cuts, the FDA's ability to hire and retain key personnel and accept the payment of user fees, and other events that may otherwise affect the FDA's ability to perform routine functions. Average review times at the FDA have fluctuated in recent years as a result. In addition, government funding of other government agencies that fund research and development activities is subject to the political process, which is inherently fluid and unpredictable. The ability of the FDA and other government agencies to properly administer their functions is highly dependent on the levels of government funding and the ability to fill key leadership appointments, among various factors. Delays in filling or replacing key positions could significantly impact the ability of the FDA and other agencies to fulfill their functions and could greatly impact healthcare and the drug industry. Disruptions at the FDA and other agencies may also slow the time necessary for new drugs and biologics or modifications to approved drugs and biologics to be reviewed and/or approved by necessary government agencies, which would adversely affect our business. For example, over the last several years, the U.S. government has shut down several times and certain regulatory agencies, such as the FDA, have had to furlough critical FDA employees and stop critical activities. If disruptions at the FDA or other agencies occurs, such as those resulting from a restructuring of these agencies, a prolonged government shutdown, or uncertainty regarding U.S. federal government funding, could significantly affect the ability of the FDA to review and process our regulatory submissions in a timely manner, or other factors prevent the FDA or other regulatory authorities from conducting their regular inspections, reviews or other regulatory activities, it could significantly impact the ability of the FDA or other regulatory authorities to timely review and process our regulatory submissions, which could have a material adverse effect on our business.

In addition, a reduction or delay in government funding of research and development may adversely affect our business. For example, we have entered into a Clinical Trial Agreement with the NIDDK of the NIH to collaborate on a company-

sponsored multiple-ascending dose trial of atumelnant in ADCS. Government funding of research and development is subject to the political process, which is inherently fluid and unpredictable. Government proposals to reduce or eliminate budgetary deficits have sometimes included reduced allocations to the NIH and other government agencies that fund research and development activities, or NIH funding may not be directed towards our products and studies, both of which could adversely affect our business and our financial results.

Further, in June 2024, the U.S. Supreme Court reversed its longstanding approach under the Chevron doctrine, which provided for judicial deference to regulatory agencies, including the FDA. As a result of this decision, we cannot be sure whether there will be increased challenges to existing agency regulations or how lower courts will apply the decision in the context of other regulatory schemes without more specific guidance from the U.S. Supreme Court. For example, this decision may result in more companies bringing lawsuits against the FDA to challenge longstanding decisions and policies of the FDA, which could undermine the FDA's authority, lead to uncertainties in the industry, and disrupt the FDA's normal operations, which could impact the timely review of any regulatory filings or applications we submit to the FDA.

The commercial success of PALSONIFY and our other product candidates, if approved, will depend upon the degree of market acceptance by physicians, patients, health care payors and others in the medical community.

PALSONIFY and our other product candidates may not be commercially successful and may not gain market acceptance among physicians, patients, healthcare payors or the medical community. The commercial success of PALSONIFY and our other current or future product candidates, if approved, will depend significantly on the broad adoption and use of the resulting product by physicians and patients for approved indications. The degree of market acceptance of our products will depend on a number of factors, including:

- demonstration of clinical efficacy and safety compared to other more-established products;
- our ability to differentiate our product against other approved products;
- the indications for which our product candidates are approved;
- the limitation of our targeted patient population and other limitations or warnings contained in any labeling approved by the FDA or other applicable regulatory authorities;
- acceptance of a new drug for the relevant indication by healthcare providers and their patients;
- the relative convenience and ease of administration of our products;
- the pricing and cost-effectiveness of our products, as well as the cost of treatment with our products in relation to alternative treatments and therapies;
- our ability to obtain and maintain sufficient third-party coverage and adequate reimbursement from government healthcare programs, including Medicare and Medicaid, private health insurers and other third-party payors;
- the willingness of patients to pay all, or a portion of, out-of-pocket costs associated with our products in the absence of sufficient third-party coverage and adequate reimbursement;
- the prevalence and severity of any adverse effects;
- potential product liability claims;
- the timing of regulatory approvals and market introduction of our products as well as competitive drugs;
- the terms of any approvals and the countries in which approvals are obtained;
- the effectiveness of our or any of our potential future collaborators' sales and marketing strategies; and
- the public perception regarding any products we may develop.

If any product does not achieve an adequate level of acceptance by physicians, hospitals, healthcare payors or patients, we may not generate sufficient revenue from that product and may not become or remain profitable. Our efforts to educate the medical community and third-party payors regarding the benefits of our products may require significant resources and may never be successful, which could have material adverse effect on our business, prospectus, reputation and financial condition.

The successful commercialization of PALSONIFY and, if approved, our other product candidates, will depend in part on the extent to which governmental authorities and health insurers establish coverage, adequate reimbursement levels and favorable pricing policies. Failure to obtain or maintain coverage and adequate reimbursement for our products could limit our ability to market those products and decrease our ability to generate revenue.

The availability of coverage and the adequacy of reimbursement by governmental healthcare programs such as Medicare and Medicaid, private health insurers and other third-party payors are essential for most patients to be able to afford prescription medications such as PALSONIFY and, if approved, our other product candidates. Our ability to achieve coverage and acceptable levels of reimbursement for our products by governmental authorities, private health insurers and other organizations will have an effect on our ability to successfully commercialize those products. Even if we obtain coverage for a given product by a third-party payor, the resulting reimbursement payment rates may not be adequate or may require co-payments that patients find unacceptably high. We cannot be sure that coverage and reimbursement in the

U.S., the European Union or elsewhere will be available for any product that we may develop, and any reimbursement that may become available may be decreased or eliminated in the future.

Third-party payors increasingly are challenging prices charged for pharmaceutical products and services, and many third-party payors may refuse to provide coverage and reimbursement for particular drugs when an equivalent generic drug or a less expensive therapy is available. It is possible that a third-party payor may consider our products as substitutable and only offer to reimburse patients for the less expensive product. Even if we are successful in demonstrating improved efficacy or improved convenience of administration with our products, pricing of existing drugs may limit the amount we will be able to charge for our products. These payors may deny or revoke the reimbursement status of a given product or establish prices for new or existing marketed products at levels that are too low to enable us to realize an appropriate return on our investment in product development. If reimbursement is not available or is available only at limited levels, we may not be able to successfully commercialize our products and may not be able to obtain a satisfactory financial return on products that we may develop.

There is significant uncertainty related to the insurance coverage and reimbursement of newly approved products. In the U.S., third-party payors, including private and governmental payors play an important role in determining the extent to which new drugs will be covered. Some third-party payors may require pre-approval of coverage for new or innovative devices or drug therapies before they will reimburse health care providers who use such therapies. It is difficult to predict at this time what third-party payors will decide with respect to the coverage and reimbursement for our products.

Obtaining and maintaining reimbursement status is time-consuming, costly and uncertain. The Medicare and Medicaid programs increasingly are used as models for how private payors and other governmental payors develop their coverage and reimbursement policies for drugs. However, no uniform policy for coverage and reimbursement for products exists among third-party payors in the U.S. In addition, international drug pricing policy changes may result in pricing pressures that could materially impact revenue. Therefore, coverage and reimbursement for products can differ significantly from payor to payor. As a result, the coverage determination process is often a time-consuming and costly process that will require us to provide scientific and clinical support for the use of our products to each payor separately, with no assurance that coverage and adequate reimbursement will be applied consistently or obtained in the first instance. Furthermore, rules and regulations regarding reimbursement change frequently, in some cases at short notice, and we believe that changes in these rules and regulations are likely.

Outside the U.S., international operations are generally subject to extensive governmental price controls and other market regulations, and we believe the increasing emphasis on cost-containment initiatives in Europe and other countries has and will continue to put pressure on the pricing and usage of our products. In many countries, the prices of medical products are subject to varying price control mechanisms as part of national health systems. Other countries allow companies to fix their own prices for medical products but monitor and control company profits. Changes in pricing regulation and exchange rates could restrict the amount that we are able to charge for our products. Accordingly, in markets outside the U.S., the reimbursement for our products may be reduced compared with the U.S. and may be insufficient to generate commercially reasonable revenue and profits.

Moreover, increasing efforts by governmental and third-party payors in the U.S. and abroad to cap or reduce healthcare costs may cause such organizations to limit both coverage and the level of reimbursement for newly approved products and, as a result, they may not cover or provide adequate payment for our products. We expect to experience pricing pressures in connection with the sale of any of our products due to the trend toward managed healthcare, the increasing influence of health maintenance organizations and additional legislative changes and reform efforts. The downward pressure on healthcare costs in general, particularly prescription drugs and surgical procedures and other treatments, has become very intense. In addition, communications from government officials, media outlets, and others regarding health care costs and pharmaceutical pricing could have a negative impact on our stock price, even if such communications do not ultimately impact coverage or reimbursement decisions for our products.

We face competition from entities that have developed or may develop somatostatin agonist products and other competitive candidates. If these companies develop competing technologies or product candidates more rapidly than we do or their technologies are more effective, our ability to develop and successfully commercialize products may be adversely affected.

The biotechnology and pharmaceutical industries are characterized by rapidly advancing technologies, intense competition and a strong emphasis on proprietary and novel products and product candidates. Our competitors have developed, are developing or may develop products, product candidates and processes competitive with our product candidates. Any product candidates that we successfully develop and commercialize will compete with existing therapies and new therapies that may become available in the future. We believe that a significant number of products are currently under development, and may become commercially available in the future, for the treatment of conditions for which we may attempt to develop product candidates, and which may lead us to abandon one or more product candidates, indications, or territories. In

particular, there is intense competition in the field of endocrine disorders. Our competitors include larger and better funded pharmaceutical, biopharmaceutical, biotechnological and therapeutics companies. Moreover, we may also compete with universities and other research institutions who may be active in endocrinology research and could be in direct competition with us. We also compete with these organizations to recruit management, scientists and clinical development personnel, which could negatively affect our level of expertise and our ability to execute our business plan. We will also face competition in establishing clinical trial sites, enrolling subjects for clinical trials and in identifying and in-licensing new product candidates. Smaller or early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies.

With respect to paltusotine, injected peptide somatostatin agonists and GH receptor antagonists are the main medical therapies for acromegaly patients where surgery is unsuccessful. There are three injected somatostatin analogs approved for the treatment of acromegaly: octreotide (marketed by Novartis AG), lanreotide (marketed by Ipsen Biopharmaceuticals, Inc.) and pasireotide (marketed by Recordati Rare Diseases Inc.). Oral octreotide (marketed by Chiesi Farmaceutici) is approved in the U.S. for the long-term maintenance treatment in acromegaly patients who have responded to and tolerated treatment with octreotide or lanreotide. Pegvisomant (marketed by Pfizer Inc.) is a daily injectable GHRA and is generally used in patients not fully controlled on somatostatin analogs. Orally administered dopamine agonists, such as bromocriptine and cabergoline, are also used.

In December 2021, the FDA approved a biosimilar of lanreotide injection, followed by the approval of a generic lanreotide injection in May 2024 for the treatment of acromegaly, CS, and GEP-NETs. Both products are manufactured by Cipla Ltd. Additionally, in December 2023, the FDA approved an octreotide acetate injectable suspension for treating acromegaly and CS. Other products in clinical development include new formulations of peptide somatostatin agonists (Camurus AB) and GH receptor antagonists (Alexion Pharmaceuticals, Inc./AstraZeneca PLC).

Injected depots of peptide somatostatin analogs are used as therapy for NETs. In adults whose CS symptoms are inadequately controlled by somatostatin therapy, telotristat ethyl (marketed by TerSera Therapeutics, Inc.) is an orally administered add-on therapy. In 2018, the FDA approved Novartis' Lutathera for the treatment of somatostatin receptor-positive GEP-NETs. Camurus AB, Chiesi Farmaceutici, POINT Biopharma Global Inc., Exelixis, RayzeBio, and ITM Isotopen Technologien Munchen are currently engaged in Phase 3 trials of new compounds for use in the treatment of NETs and/or CS symptoms. Other companies developing NETs therapeutics that target somatostatin receptors include Oranomed/RadioMedix, ASCIL Biopharm, Molecular Targeting Technologies Inc., Perspective Therapeutics, and Immunwork Inc. We also face competition from therapies with different mechanisms of action and routes of administration, including PRRT, cytotoxic chemotherapy, and targeted therapies such as mTOR inhibitors and tyrosine kinase inhibitors.

As with acromegaly, first-line therapy for Cushing's disease is surgery to remove the pituitary tumor if possible. The use of adrenal enzyme inhibitors (metyrapone, ketoconazole and more recently levoketoconazole which gained FDA approval in December 2021 and is marketed by Xeris Pharmaceuticals) prevent the synthesis of cortisol and can improve symptoms. Mifepristone (marketed by Corcept Therapeutics, Inc.), a glucocorticoid receptor antagonist, is approved for control of hyperglycemia in Cushing's syndrome. A generic form of mifepristone has been approved for the treatment of endogenous Cushing's syndrome. Osilodrostat (marketed by Recordati Rare Diseases Inc.), a cortisol synthesis inhibitor, is approved for the treatment of endogenous Cushing's syndrome. The somatostatin agonist pasireotide is also approved for Cushing's disease. Other companies developing products for potential use in Cushing's disease include Corcept Therapeutics, Inc., Sparrow Pharmaceuticals, and Lundbeck Pharmaceuticals. In December 2024, the FDA approved CRF1 receptor antagonist, crinecerfont (marketed by Neurocrine Biosciences) for the treatment of classic CAH and Neurocrine Biosciences is also developing a peptide CRF receptor antagonist for CAH.

Many of our competitors have significantly greater financial, technical, manufacturing, marketing, sales and supply resources or experience than we do. We face competition based on many different factors, including the safety and effectiveness of our products, the ease with which our products can be administered and the extent to which patients accept relatively new routes of administration, the timing and scope of regulatory approvals for these products, the availability and cost of manufacturing, marketing and sales capabilities, price, reimbursement coverage and patent position. Competing products could present superior treatment alternatives, including by being more effective, safer, more convenient, less expensive or marketed and sold more effectively than any products we may develop. Competitive products may make any products we develop obsolete or noncompetitive before we recover the expense of developing and commercializing our product candidates. For example, a competitor could develop another oral formulation of a somatostatin agonist or other technology that could make administration of peptide therapies more convenient. If we are unable to compete effectively, our opportunity to generate revenue from the sale of our products we may develop, if approved, could be material and adversely affected, which would material adversely affect our results of operations, financial condition and business.

The numbers of patients suffering from the rare endocrine diseases and endocrine-related tumors that we target is small and have not been established with precision. If the market opportunities for our products are smaller than we believe they are, our revenue may be adversely affected, and our business may suffer.

We have focused our research and product development on treatments for orphan and rare diseases. Given the small number of patients who have the diseases that we are targeting, it is critical to our ability to grow and become profitable that we continue to successfully identify patients with these diseases. Our projections of both the number of people who have these diseases, as well as the subset of people with these diseases who have the potential to benefit from treatment with our products, are based on our beliefs and estimates. These estimates have been derived from a variety of sources, including scientific literature, surveys of clinics, patient foundations or market research, and may prove to be incorrect. Further, new studies may change the estimated incidence or prevalence of these diseases. The number of patients may turn out to be lower than expected. If any of our estimates are inaccurate, the market opportunities for any of our product candidates could be significantly diminished. Additionally, the potentially addressable patient population for each of our products may be limited or may not be amenable to treatment with our products, and new patients may become increasingly difficult to identify or gain access to. Further, even if we obtain significant market share for our products, because the potential target populations are very small, we may never achieve profitability despite obtaining such significant market share. Any of the foregoing would materially and adversely affect our results of operations and our business.

We have sought and may continue to seek to enter into collaborations, licenses and other similar arrangements of our product and may not be successful in doing so, and even if we are, we may not realize the benefits of such relationships.

We have sought and may continue to seek to enter into collaborations, licenses and other similar arrangements for the development or commercialization of our product candidates, such as the SKK License, due to capital costs required to develop or commercialize the product candidate in certain markets. Any such arrangements may also be subject to the additional risks as discussed below under the section "Risks related to our reliance on third parties." We may not be successful in our efforts to establish such collaborations for our product candidates because our product candidates may be deemed to be at too early of a stage of development for collaborative effort or third parties may not view our product candidates as having the requisite potential to demonstrate safety and efficacy or significant commercial opportunity. In addition, we face significant competition in seeking appropriate strategic partners, and the negotiation process can be time-consuming and complex. Further, we may have to relinquish valuable rights to our future revenue streams, research programs or product candidates, or grant licenses on terms that may not be favorable to us, as part of any such arrangement, and such arrangements may restrict us from entering into additional agreements with potential collaborators. We cannot be certain that, following a strategic transaction or license, we will achieve an economic benefit that justifies such transaction.

Even if we are successful in our efforts to establish such collaborations, the terms that we agree upon may not be favorable to us, and we may not be able to maintain such collaborations if, for example, development or approval of a product candidate is delayed, the safety of a product candidate is questioned, or sales of an approved product are unsatisfactory. We also may not be able to realize the benefit of such collaborations if we are unable to successfully integrate them with our existing operations and company culture.

In addition, any potential future collaborations may be terminable by our strategic partners, and we may not be able to adequately protect our rights under these agreements. Furthermore, strategic partners may negotiate for certain rights to control decisions regarding the development and commercialization of our product candidates, if approved, and may not conduct those activities in the same manner as we do. Any termination of collaborations we enter into in the future, or any delay in entering into collaborations related to our product candidates, could delay the development and commercialization of our product candidates and reduce their competitiveness if they reach the market, which could have a material adverse effect on our business, financial condition and results of operations.

We obtained regulatory approval from the FDA for PALSONIFY but have limited demonstration of conducting commercial activities.

We received FDA approval for PALSONIFY (paltusotine) for the treatment of acromegaly on September 25, 2025. Prior to obtaining this approval, our operations were limited to financing and staffing our company, developing our technology, conducting preclinical research and clinical trials of our product candidates and preparing for a commercial launch. We have not received regulatory approval or commercialized any other product candidates to date and may never do so. We have not yet demonstrated an ability to conduct long-term sales and marketing activities necessary for successful product commercialization. Accordingly, our stockholders should consider our prospects in light of the costs, uncertainties, delays in product uptake and coverage and other difficulties frequently encountered by biopharmaceutical companies such as ours. Any predictions made about our future success or viability may not be as accurate as they could be if we had a longer operating history or a history of successfully commercializing pharmaceutical products.

The manufacturing, labeling, packaging, distribution, adverse event reporting, storage, advertising, promotion, sampling, and record keeping related to our product will remain subject to extensive regulatory requirements. These requirements include submissions of safety and other post-marketing information and reports, registration, as well as continued compliance with cGMP regulations, and GCPs for any clinical trials that we conduct post-approval, all of which may result in significant expense and limit our ability to commercialize PALSONIFY. As such, we and our contract manufacturers will be subject to periodic review and inspections to assess compliance with cGMP and adherence to commitments made in any NDA or other marketing application and previous responses to inspection observations. For certain commercial prescription drug products, manufacturers and other parties involved in the supply chain must also meet chain of distribution requirements and build electronic, interoperable systems for product tracking and tracing and for notifying the FDA of counterfeit, diverted, stolen and intentionally adulterated products or other products that are otherwise unfit for distribution in the U.S. Accordingly, we and others with whom we work must continue to expend time, money, and effort in all areas of regulatory compliance, including manufacturing, production and quality control.

We may encounter unforeseen expenses, difficulties, complications, delays and other known or unknown factors in achieving our business objectives. We will need to continue to transition from a company with a development focus to a company capable of supporting commercial activities. We may not be successful in such a transition. We expect our financial condition and operating results to continue to fluctuate significantly from quarter to quarter and year to year.

Our future growth may depend, in part, on our ability to operate in foreign markets, where we would be subject to additional regulatory burdens and other risks and uncertainties.

Our future growth may depend, in part, on our ability to develop and commercialize our product candidates in foreign markets. We are not permitted to market or promote any of our product candidates before we receive regulatory approval from applicable regulatory authorities in foreign markets, and we may never receive such regulatory approvals for any of our product candidates. To obtain separate regulatory approval in many other countries we must comply with numerous and varying regulatory requirements regarding safety and efficacy and governing, among other things, clinical trials, commercial sales, pricing and distribution of our product candidates. Obtaining and maintaining marketing approval of our current and future product candidates in one jurisdiction does not guarantee that we will be able to obtain or maintain marketing approval in any other jurisdiction, while a failure or delay in obtaining marketing approval in one jurisdiction may have a negative effect on the marketing approval process in others. If we obtain regulatory approval of our product candidates and ultimately commercialize our products in foreign markets, we would be subject to additional risks and uncertainties, any of which could result in a material adverse effect on our business, prospectus and results of operations, including:

- different regulatory requirements for approval of drugs in foreign countries;
- reduced protection for intellectual property rights;
- the existence of additional third-party patent rights of potential relevance to our business;
- changes in tariffs, trade barriers, regulatory requirements, the implementation of rebate models such as the Guarding U.S. Medicare Against Rising Drug Costs (GUARD) Model or the GENEROUS (GENErating cost Reductions for U.S. Medicaid) Model, should either of those become applicable to Crinetics products;
- economic weakness, including inflation, or political instability in domestic and particular foreign economies and markets;
- compliance with tax, employment, immigration and labor laws for employees living or traveling abroad;
- foreign currency fluctuations, which could result in increased operating expenses and reduced revenue, and other obligations incident to doing business in another country;
- foreign reimbursement, pricing and insurance regimes;
- workforce uncertainty in countries where labor unrest is common;
- production shortages resulting from any events affecting raw material supply or manufacturing capabilities abroad; and
- business interruptions resulting from geopolitical actions, including war and terrorism, or natural disasters including earthquakes, typhoons, floods and fires.

Risks related to our reliance on third parties

We rely on third parties to conduct many of our preclinical studies and clinical trials. Any failure by a third party to conduct the clinical trials according to GCPs and in a timely manner may delay or prevent our ability to seek or obtain regulatory approval for or commercialize our product candidates.

We are dependent on third parties to conduct our preclinical studies and clinical trials, including our clinical trials for paltusotine, atumelnant, and any future clinical trials and preclinical studies for our product candidates. For example, we have used and relied on, and intend to continue to use and rely on, medical institutions, clinical investigators, partners, licensees, clinical data management organizations, CROs, trial sites, and consultants, among others, to conduct our clinical

trials in accordance with our trial design, clinical protocols and regulatory requirements. These CROs, investigators and other third parties play a significant role in the conduct and timing of these trials and subsequent collection and analysis of data. While we have agreements governing the activities of our third-party contractors, we have limited influence over their actual performance. Nevertheless, we are responsible for ensuring that each of our pre-clinical and clinical trials is conducted in accordance with the applicable protocol and legal, regulatory and scientific standards, and our reliance on the CROs and other third parties does not relieve us of our regulatory responsibilities. We and our CROs are required to comply with GCP requirements, which are regulations and guidelines enforced by the FDA and comparable foreign regulatory authorities for all of our product candidates in clinical development. We must also ensure that our preclinical trials are conducted in accordance with the FDA's Good Laboratory Practice regulations, as appropriate. Regulatory authorities enforce these requirements through periodic inspections of trial sponsors, principal investigators and trial sites. If we or any of our CROs or trial sites fail to comply with applicable GCPs, the clinical data generated in our clinical trials may be deemed unreliable, and the FDA or comparable foreign regulatory authorities may require us to perform additional clinical trials before approving our marketing applications. In addition, our clinical trials must be conducted with product produced under cGMP regulations. Our failure to comply with these regulations may require us to repeat clinical trials, which would delay the regulatory approval process.

There is no guarantee that any such CROs, investigators or other third parties will devote adequate time and resources to such trials or perform as contractually required. If any of these third parties fail to meet expected deadlines, adhere to our clinical protocols or meet regulatory requirements, or otherwise performs in a substandard manner, our clinical trials may be extended, delayed or terminated. In addition, many of the third parties with whom we contract may also have relationships with other commercial entities, including our competitors, for whom they may also be conducting clinical trials or other drug development activities that could harm our competitive position.

If any of our relationships with these third parties terminate, we may not be able to enter into arrangements with alternative third parties or do so on commercially reasonable terms or in a time frame acceptable to us. Even if we are able to enter into alternative arrangements, switching or adding additional CROs, investigators and other third parties involves additional cost and requires management time and focus. In addition, there is a natural transition period when a new CRO commences work. As a result, delays occur, which can materially impact our ability to meet our desired clinical development timelines. Though we carefully manage our relationships with our CROs, investigators and other third parties, there can be no assurance that we will not encounter challenges or delays in the future or that these delays or challenges will not have a material adverse impact on our business, financial condition and prospects.

We rely on third parties for raw materials, active pharmaceutical ingredients, and drug product intermediates for the manufacture of our product candidates for preclinical and clinical development and expect to continue to do so for the foreseeable future. This reliance on third parties increases the risk that we will not have sufficient quantities of our product candidates or products or such quantities at an acceptable cost, which could delay, prevent or impair our development or commercialization efforts.

We do not own or operate manufacturing facilities and have no plans to build our own clinical or commercial scale manufacturing capabilities. We rely, and expect to continue to rely, on third parties for the manufacture and supply of our product candidates and related raw materials for preclinical and clinical development, as well as for commercial manufacture of PALSONIFY and any of our product candidates that receive marketing approval. Furthermore, the raw materials for our product candidates are sourced, in some cases, from a single-source supplier. If we were to experience an unexpected loss of or interruption to supply of any of our product candidates or any of our future product candidates for any reason, whether as a result of manufacturing, supply or storage issues or otherwise, we could experience delays, disruptions, suspensions or terminations of, or be required to restart or repeat, any pending or ongoing clinical trials.

We will depend on these third parties to perform their obligations in a timely manner consistent with contractual and regulatory requirements, including those related to quality control and assurance. For example, the facilities used by third-party manufacturers to manufacture our product candidates must be approved by the FDA pursuant to inspections that will be conducted after we submit our NDA to the FDA. We do not control the manufacturing process of, and are completely dependent on, third-party manufacturers for compliance with cGMP requirements for manufacture of drug products. If these third-party manufacturers cannot successfully manufacture material that conforms to our specifications and the strict regulatory requirements of the FDA or others, including requirements related to the manufacturing of high potency compounds, they will not be able to secure and/or maintain regulatory approval for their manufacturing facilities. In addition, we have no control over the ability of third-party manufacturers to maintain adequate quality control, quality assurance and qualified personnel. If the FDA or a comparable foreign regulatory authority does not approve these facilities for the manufacture of our product candidates or if it withdraws any such approval in the future, we may need to find alternative manufacturing facilities, which would significantly impact our ability to develop, obtain regulatory approval for or market our product candidates if approved. Our failure, or the failure of our third-party manufacturers, to comply with applicable regulations could result in sanctions being imposed on us, including clinical holds, fines, injunctions, civil

penalties, delays, suspension or withdrawal of approvals, seizures or recalls of product candidates or products, operating restrictions and criminal prosecutions, any of which could significantly and adversely affect supplies of our products.

Any performance failure on the part of our existing or future manufacturers could delay clinical development or marketing approval, and any related remedial measures may be costly or time-consuming to implement. We do not currently have arrangements in place for redundant supply or a second source for all required raw materials, active pharmaceutical ingredients, and drug product intermediaries used in the manufacture of our product candidates. If our current third-party suppliers and manufacturers cannot perform as agreed, we may be required to replace such third parties, and we may be unable to replace them on a timely basis or at all.

If we are required to change suppliers or manufacturers for any reason, we will be required to verify that the new manufacturer maintains facilities and procedures that comply with quality standards and with all applicable regulations and guidelines. In addition, we may be unable to establish any agreements with third-party suppliers or manufacturers or to do so on acceptable terms. The delays associated with the onboarding of a new manufacturer could negatively affect our ability to develop product candidates in a timely manner or within budget. Even if we are able to establish agreements with third-party manufacturers, reliance on third-party suppliers and manufacturers entails additional risks, including:

- failure of third-party suppliers and manufacturers to comply with regulatory requirements and maintain quality assurance;
- breach of the supply or manufacturing agreement by the third party;
- failure to supply or manufacture our product according to our specifications, to our schedule or at all;
- failure of third-party suppliers and manufacturers to maintain a sufficient supply of materials and ingredients necessary to conduct their operations;
- inability of a third-party manufacturer to scale up the process in order to produce commercial quantities of our products if approved;
- misappropriation of our proprietary information, including our trade secrets and know-how;
- termination or nonrenewal of the agreement by the third party at a time that is costly or inconvenient for us; and
- changes in international trade policies, international conflicts, or any other external events that may impact the ability of our third-party supplier and manufacturer located outside of the U.S. to perform and to manufacture our product.

Our product candidates and any products that we may develop may compete with other product candidates and products for access to manufacturing facilities. There are a limited number of manufacturers that operate under cGMP regulations and that might be capable of manufacturing for us.

Our current and anticipated future dependence upon others for the manufacture of our product candidates or products may materially and adversely affect our future profit margins and our ability to commercialize any products that receive marketing approval on a timely and competitive basis, which would have a material adverse effect on our business, reputation and prospects.

We are dependent on an international third-party licensee for the development and commercialization of paltusotine in Japan, and we may enter into similar agreements in other geographic regions. The failure of this and other third parties to meet their contractual, regulatory or other obligations could adversely affect our business.

We have entered into an exclusive license agreement with SKK that provides SKK with exclusive rights to the development and commercialization of paltusotine in Japan. As a result, we are dependent on SKK to achieve regulatory approval of paltusotine for marketing in Japan and for the commercialization of paltusotine in Japan, if approved. The timing and amount of any milestone and royalty payments we may receive under this agreement will depend on, among other things, the efforts and allocation of resources and successful commercialization of paltusotine in Japan by SKK. We also depend on SKK to comply with all applicable laws related to the development and commercialization of our product in Japan. For example, they may take actions or fail to take actions that result in safety issues with the licensed product in the licensed territory, and such safety issues could negatively impact the licensed product in countries outside of the licensed territory. We do not control the individual efforts of SKK, and we have limited ability to terminate these agreements or to have assigned assets returned to us if SKK does not perform as anticipated. The failure of SKK to devote sufficient time and effort to the development and commercialization of paltusotine; to meet its obligations to us, including for future royalty and milestone payments; to adequately deploy business continuity plans in the event of a crisis; or to satisfactorily resolve significant disagreements with us or address other factors could have an adverse impact on our financial results and operations. In addition, if SKK violates, or is alleged to have violated, any laws or regulations during the performance of its obligations for us, including with respect to safety, patient and data privacy, antitrust, and bribery and corruption, it is possible that we could suffer financial and reputational harm or other negative outcomes, including possible legal consequences and liabilities. We may not be successful in enforcing the terms and conditions of our license agreement in court or via agreed upon dispute resolution mechanisms, and even if we were to prevail in any such dispute, the remedies

may not be adequate to compensate us for the losses. Any termination, breach or expiration of any of this license agreement could have a material adverse effect on our financial position by reducing or eliminating the potential for us to receive license fees, milestones and royalties. In such an event, we may be required to devote additional efforts and to incur additional costs associated with pursuing regulatory approval and commercialization of the applicable products and product candidates in Japan. Alternatively, we may attempt to identify and transact with a new assignee or licensee, but there can be no assurance that we would be able to identify a suitable partner or transact on terms that are favorable to us. In addition, we may enter into similar license agreements with additional third parties for paltusotine or our other product candidates in other geographic regions, and similar risks would be associated with any such similar arrangements.

Our reliance on third parties requires us to share our trade secrets, which increases the possibility that a competitor will discover them or that our trade secrets will be misappropriated or disclosed.

Because we currently rely on other third parties in the discovery, development, and manufacture of our product candidates, we must, at times, share our proprietary technology and confidential information, including trade secrets, with them. We seek to protect our proprietary technology, in part, by entering into non-disclosure and confidentiality agreements, consulting agreements or other similar agreements with our advisors, employees, consultants, contractors, investigators, advisors, collaborators, manufacturers, suppliers, and other third parties prior to disclosing proprietary information. These agreements typically limit the rights of the third parties to use or disclose our confidential information. For example, these agreements typically restrict the ability of the third parties to publish data potentially relating to our trade secrets, although our agreements may contain certain limited publication rights. For example, any academic institution that we may collaborate with in the future may be granted rights to publish data arising out of such collaboration, subject to certain notice and publication delay requirements in order for us to secure patent protection of intellectual property rights arising from the collaboration, in addition to the opportunity to remove confidential or trade secret information from any such publication. Despite the contractual provisions employed when working with third parties, the need to share trade secrets and other confidential information increases the risk that such trade secrets become known by our competitors, are intentionally or inadvertently incorporated into the technology of others or are disclosed or used in violation of these agreements. Given that our proprietary position is based, in part, on our know-how and trade secrets and despite our efforts to protect our proprietary information, a competitor's discovery of our proprietary technology and confidential information or other unauthorized use or disclosure would impair our competitive position and may have a material adverse effect on our business, financial condition, results of operations and prospects.

Risks related to our business operations and industry

We are dependent on the services of our management and other clinical and scientific personnel, and if we are not able to retain these individuals or recruit additional management or clinical and scientific personnel, our business will suffer.

Our success depends in part on our continued ability to attract, retain and motivate highly qualified management, clinical and scientific personnel. We are highly dependent upon our senior management, particularly our Chief Executive Officer, as well as our senior scientists and other members of our senior management team. The loss of services of any of these individuals could delay or prevent the successful development of our product pipeline, initiation or completion of our planned clinical trials or the commercialization of our product candidates. Although we have executed employment agreements or offer letters with each member of our senior management team, these agreements are terminable at will with or without notice, and therefore, we may not be able to retain their services as expected. For example, in August 2024, our prior Chief Financial Officer notified the Company of his decision to step down from the company after his replacement had been on-boarded with the Company, and in February 2025, we appointed a new Chief Financial Officer. We may not always be able to attract suitable candidates to fill similar positions in a timely manner. We also do not currently maintain "key person" life insurance on the lives of our executives or any of our employees. This lack of insurance means that we may not have adequate compensation for the loss of the services of these individuals.

We will need to expand and effectively manage our managerial, operational, financial and other resources in order to successfully pursue our clinical development and commercialization efforts. We may not be successful in maintaining our unique company culture and continuing to attract or retain qualified management and scientific and clinical personnel in the future due to the intense competition for qualified personnel among pharmaceutical, biotechnology and other businesses, particularly in the San Diego area. Our industry has experienced a high rate of turnover of management personnel in recent years, and many of the companies that we compete against for qualified personnel have greater financial and other resources, different risk profiles and a longer history in the industry than we do. If we are not able to attract, integrate, retain and motivate necessary personnel to accomplish our business objectives, we may experience constraints that will significantly impede the achievement of our development objectives, our ability to raise additional capital and our ability to implement our business strategy.

We may encounter difficulties in managing our growth and expanding our operations successfully.

As of February 13, 2026, we had 594 full-time employees. As we continue commercialization of PALSONIFY and the development and potential commercialization of our product candidates, as well as function as a public company, we will need to continue expanding our financial, development, regulatory, manufacturing, operational, marketing and sales capabilities or contract with third parties to provide these capabilities for us. To manage our anticipated future growth, we may need to improve existing and implement new managerial, operational and financial processes, expand our facilities and recruit and train additional qualified personnel. As our operations expand, we expect that we will need to manage additional relationships with various strategic partners, suppliers and other third parties. Our future financial performance and our ability to develop and commercialize our products and product candidates and to compete effectively will depend, in part, on our ability to manage any future growth effectively, which would have a material adverse effect on our business.

We are subject to various foreign, federal and state healthcare laws and regulations, and our failure to comply with these laws and regulations could harm our results of operations and financial condition.

Our business operations and current and future arrangements with investigators, healthcare professionals, consultants, advisors, third-party payors and customers expose us to broadly applicable federal and state fraud and abuse and other healthcare laws and regulations. These laws may constrain the business or financial arrangements and relationships through which we conduct our operations, including how we research, market, sell and distribute any products for which we obtain marketing approval. Such laws include:

- the federal Anti-Kickback Statute, which prohibits, among other things, persons or entities from knowingly and willfully soliciting, offering, receiving or providing any remuneration (including any kickback, bribe or certain rebates), directly or indirectly, overtly or covertly, in cash or in kind, in return for, either the referral of an individual or the purchase, lease, or order, or arranging for or recommending the purchase, lease, or order of any good, facility, item or service, for which payment may be made, in whole or in part, under a federal healthcare program such as Medicare and Medicaid. A person or entity does not need to have actual knowledge of the federal statute or specific intent to violate it in order to have committed a violation;
- the federal false claims, including the civil False Claims Act, which, among other things, impose criminal and civil penalties against individuals or entities for knowingly presenting, or causing to be presented, to the federal government, claims for payment or approval that are false or fraudulent, knowingly making, using or causing to be made or used, a false record or statement material to a false or fraudulent claim, or from knowingly making or causing to be made a false statement to avoid, decrease or conceal an obligation to pay money to the federal government. In addition, the government may assert that a claim including items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the civil False Claims Act;
- HIPAA, which imposes criminal and civil liability for, among other things, knowingly and willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program, or knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false statement, in connection with the delivery of, or payment for, healthcare benefits, items or services. Similar to the federal Anti-Kickback Statute, a person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation.
- the federal Physician Payments Sunshine Act, which requires certain manufacturers of drugs, devices, biologics and medical supplies for which payment is available under Medicare, Medicaid or the Children's Health Insurance Program (with certain exceptions) to report annually to the government information related to payments and other "transfers of value" made to physicians (defined to include doctors, dentists, optometrists, podiatrists and chiropractors), certain other healthcare professionals (physician assistants, nurse practitioners, clinical nurse specialists, anesthesiologist assistants, certified registered nurse anesthetists, anesthesiology assistants and certified nurse midwives), and teaching hospitals, as well as ownership and investment interests held by the physicians described above and their immediate family members; and
- analogous state and foreign laws and regulations, such as state anti-kickback and false claims laws, which may apply to our business practices, including but not limited to, research, distribution, sales and marketing arrangements and claims involving healthcare items or services reimbursed by non- governmental third-party payors, including private insurers, or by the patients themselves; state laws that require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government, or otherwise restrict payments that may be made to healthcare providers and other potential referral sources; state laws and regulations that require drug manufacturers to file reports relating to pricing and marketing information, which requires tracking gifts and other remuneration and items of value provided to physicians, other healthcare providers and entities; state and local laws that require the registration of pharmaceutical sales representatives.

Ensuring that our internal operations and business arrangements with third parties comply with applicable healthcare laws and regulations could involve substantial costs. It is possible that governmental authorities will conclude that our business practices, including our consulting and advisory board arrangements with physicians and other healthcare providers, some of whom receive stock options as compensation for services provided, do not comply with current or future statutes, regulations, agency guidance or case law involving applicable fraud and abuse or other healthcare laws and regulations. If our operations are found to be in violation of any of the laws described above or any other governmental laws and regulations that may apply to us, we may be subject to significant penalties, including civil, criminal and administrative penalties, damages, fines, exclusion from U.S. government funded healthcare programs, such as Medicare and Medicaid, or similar programs in other countries or jurisdictions, disgorgement, individual imprisonment, contractual damages, reputational harm, additional reporting requirements and oversight if we become subject to a corporate integrity agreement or similar agreement to resolve allegations of non-compliance with these laws, diminished profits and the curtailment or restructuring of our operations. Further, defending against any such actions can be costly, time-consuming and may require significant financial and personnel resources. Therefore, even if we are successful in defending against any such actions that may be brought against us, our business may be impaired. If any of the physicians or other providers or entities with whom we expect to do business are found to not be in compliance with applicable laws, they may be subject to criminal, civil or administrative sanctions, including exclusion from government funded healthcare programs and imprisonment. If any of the above occur, it could adversely affect our ability to operate our business and our results of operations.

Actual or perceived failures to comply with applicable data protection, privacy and security laws, regulations, standards and other requirements could have a material adverse effect on our business, financial condition or results of operations.

Privacy and data security have become significant issues in the U.S., E.U. and in many other jurisdictions where we may in the future conduct our operations. The legislative and regulatory landscape for privacy and data protection continues to evolve, and there has been an increasing focus on privacy and data protection issues, which may affect our business and may increase our compliance costs and exposure to liability. As we receive, collect, process, use and store personal and confidential data, we are or may be subject to diverse laws and regulations relating to data privacy and security. Compliance with these privacy and data security requirements is rigorous and time-intensive and may increase our cost of doing business, and despite those efforts, there is a risk that we may be subject to fines and penalties, litigation and reputational harm, which could materially and adversely affect our business, financial condition and results of operations.

In the U.S., we may be subject to data privacy and security regulation by both the federal government and the states in which we conduct our business. HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act, and their implementing regulations, or collectively, HIPAA, impose, among other things, certain standards relating to the privacy, security, transmission and breach reporting of individually identifiable health information held by covered entities and their business associates. We may obtain health information from third parties (including research institutions from which we obtain clinical trial data) that are subject to privacy and security requirements under HIPAA. Depending on the facts and circumstances, we could be subject to criminal penalties if we knowingly receive individually identifiable health information from a HIPAA-covered entity in a manner that is not authorized or permitted by HIPAA.

In addition, state laws govern the privacy and security of health-related and other personal information in certain circumstances, many of which differ from each other in significant ways and may not have the same requirements, thus complicating compliance efforts. By way of example, California enacted the CCPA effective January 1, 2020, which gives California residents expanded rights to access, correct, and delete their personal information, opt out of certain personal information sharing and disclosure, and receive detailed information about how their personal information is used. The CCPA provides for civil penalties for violations, as well as a private right of action for data breaches that has increased the likelihood of, and risks associated with, data breach litigation. The CCPA may increase our compliance costs and potential liability. Further, the CPRA generally went into effect on January 1, 2023, and significantly amends the CCPA. The CPRA imposes additional data protection obligations on covered businesses, including additional consumer rights processes, limitations on data uses, new audit requirements for higher risk data, and opt outs for certain uses of sensitive data. It also creates a new California data protection agency authorized to issue substantive regulations and could result in increased privacy and information security enforcement, and additional compliance investment and potential business process changes may be required. Similar laws have passed or have been proposed in other states and at the federal level, reflecting a trend toward more stringent privacy legislation in the U.S. Further states have also enacted consumer health data privacy laws, including states without comprehensive consumer privacy laws, such as Nevada and Washington state. The enactment of such laws could have potentially conflicting requirements that would make compliance challenging. In the event that we are subject to or affected by HIPAA, the CCPA, the CPRA or other domestic privacy and data protection laws, any liability from failure to comply with the requirements of these laws could adversely affect our financial condition.

In the EEA, the GDPR imposes stringent requirements for controllers and processors of personal data, including, for example, high standards for obtaining consent from individuals to process their personal data, robust disclosures to individuals and a strong individual data rights regime, short timelines for data breach notifications, limitations on retention and secondary use of information, significant requirements pertaining to health data and pseudonymized (i.e., key-coded) data and obligations when we contract third-party processors in connection with the processing of the personal data. Companies that must comply with the GDPR face increased compliance obligations and risk, including more robust regulatory enforcement of data protection requirements and potential fines for noncompliance of up to €20 million or 4% of the annual global revenue of the noncompliant company, whichever is greater. Among other requirements, the GDPR regulates transfers of personal data subject to the GDPR to third countries that have not been found to provide adequate protection to such personal data, including the U.S.; in July 2020, the CJEU invalidated the Privacy Shield, under which personal data could be transferred from the EEA to U.S. entities who had self-certified under the Privacy Shield scheme and imposed further restrictions on the use of SCCs. In March 2022, the U.S. and EU announced a new regulatory regime intended to replace the invalidated regulations with the EU-U.S. DPF. In July 2023, the European Commission adopted an adequacy decision in relation to the EU-U.S. DPF, allowing the EU-U.S. DPF to be utilized as a means of legitimizing EU-U.S. personal data transfers for participating entities. The EU-U.S. DPF may be subject to legal challenges from privacy advocacy groups or others, and the European Commission's adequacy decision regarding the EU-U.S. DPF provides that the EU-U.S. DPF will be subject to future reviews and may be subject to suspension, amendment, repeal, or limitations to its scope by the European Commission. As supervisory authorities issue further guidance on personal data export mechanisms, including circumstances where the standard contractual clauses cannot be used, and/ or start taking enforcement action, we could suffer additional costs, complaints and/ or regulatory investigations or fines, and/ or if we are otherwise unable to transfer personal data between and among countries and regions in which we operate, it could affect the manner in which we provide our services, the geographical location or segregation of our relevant systems and operations, and could adversely affect our financial results.

Additionally, since January 1, 2021, we have been subject to the GDPR and also the UK GDPR which, together with the amended UK Data Protection Act 2018, retains the GDPR in UK national law. On June 28, 2021, the European Commission adopted an adequacy decision for the UK, allowing for the relatively free exchange of personal information between the EU and the UK (as the UK correspondingly allows transfers back to the EU). However, the European Commission may suspend the adequacy decision if it considers that the UK no longer provides for an adequate level of data protection, and the decision will automatically expire in June 2025, unless it is renewed/extended. The UK GDPR mirrors the fines under the GDPR, e.g. fines up to the greater of €20 million (£17.5 million) or 4% of global turnover. In December 2024, the UK government revived its attempts to amend the UK GDPR in a new Data (Use and Access) Bill. If passed, this may lead to additional compliance costs and could increase our overall risk. The respective provisions and enforcement of the EU GDPR and UK GDPR may further diverge in the future and create additional regulatory challenges and uncertainties.

Compliance with U.S. and foreign data privacy and security laws, rules and regulations could require us to take on more onerous obligations in our contracts, require us to engage in costly compliance exercises, restrict our ability to collect, use and disclose data, or in some cases, impact our or our partners' or suppliers' ability to operate in certain jurisdictions. As we continue to expand into other foreign countries and jurisdictions, we may be subject to additional laws and regulations that may affect how we conduct business. Each of these constantly evolving laws can be subject to varying interpretations. If we fail to comply with any such laws, rules or regulations, we may face government investigations and/or enforcement actions, fines, civil or criminal penalties, private litigation or adverse publicity that could adversely affect our business, financial condition and results of operations.

Recently enacted legislation, future legislation and healthcare reform measures may increase the difficulty and cost for us to obtain marketing approval for and commercialize our products and product candidates and may affect the prices we may set.

In the U.S. and some foreign jurisdictions, there have been, and we expect there will continue to be, a number of legislative and regulatory changes to the healthcare system, including cost-containment measures that may reduce or limit coverage and reimbursement for newly approved drugs and affect our ability to profitably sell any product candidates for which we obtain marketing approval. In particular, there have been and continue to be a number of initiatives at the U.S. federal and state levels that seek to reduce healthcare costs and improve the quality of healthcare that may impact our ability to sell and receive adequate reimbursement of our product candidates.

Further, there has been heightened governmental scrutiny in the U.S. of pharmaceutical pricing practices in light of the rising cost of prescription drugs. Such scrutiny has resulted in several recent congressional inquiries and proposed and enacted federal and state legislation designed to, among other things, bring more transparency to product pricing, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for products. On August 16, 2022, the IRA was signed into law. Among other things, the IRA requires

manufacturers of certain drugs to engage in price negotiations with Medicare (beginning in 2026), with prices that can be negotiated subject to a cap; imposes rebates under Medicare Part B and Medicare Part D to penalize price increases that outpace inflation (which began in 2023); and replaces the Part D coverage gap discount program with a new discounting program (which began in 2025). The IRA permits the Secretary of the Department of Health and Human Services (HHS) to implement many of these provisions through guidance, as opposed to regulation, for the initial years. On June 30, 2023, the CMS issued new guidance detailing the requirements and parameters of the first round of price negotiations, to take place during 2023 and 2024, for products subject to the "maximum fair price" provision that would become effective in 2026. In August 2023, HHS announced the list of the first ten drugs selected for price negotiations. In August 2024, following negotiation with the manufacturers of the selected drugs, HHS announced the negotiated prices for such drugs. Although the Medicare drug price negotiation program is currently subject to legal challenges, it is likely to have a significant impact on the pharmaceutical industry and could negatively affect our business and financial condition. CMS and HHS will continue to issue and update guidance as these programs are implemented.

At the state level, individual states in the U.S. are also increasingly active in passing legislation and implementing regulations designed to control pharmaceutical and biological product pricing, including prescription drug affordability boards, price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing. Legally mandated price controls on payment amounts by third-party payors or other restrictions could harm our business, results of operations, financial condition and prospects. In addition, regional healthcare authorities and individual hospitals are increasingly using bidding procedures to determine what pharmaceutical products and which suppliers will be included in their prescription drug and other healthcare programs. This could reduce the ultimate demand for our product candidates, if approved, or put pressure on our product pricing, which could negatively affect our business, results of operations, financial condition and prospects.

We cannot predict all of the ways in which future healthcare reform legislation or regulation could affect our business, particularly in light of the current presidential administration. We expect that these new laws and other healthcare reform measures that may be adopted in the future could result in additional reductions in Medicare and other healthcare funding, more rigorous coverage criteria, new payment methodologies and additional downward pressure on the price that we receive for any approved product in the US or other countries. Any reduction in reimbursement from Medicare or other government programs may result in a similar reduction in payments from private payors. The implementation of cost containment measures or other healthcare reforms may prevent us from being able to generate revenue, attain profitability or commercialize our products and product candidates in the US or other countries, if approved, which could have a material adverse effect on our results of operations and financial condition. For example, in November 2025, CMS published a request for applications for another Center for Medicare and Medicaid Innovation (CMMI) model, the GENEROUS (GENErating cost Reductions fOr U.S. Medicaid) Model. This is a voluntary model that tests the effect of supplemental rebate agreements between manufacturers and CMS, which align Medicaid prices with a defined most favored nation (MFN) price. In addition, in December 2025, the Trump Administration announced two new CMMI models: the Global Benchmark for Efficient (GLOBE) Drug Pricing Model, which proposes MFN-based rebates in Medicare Part B; and the Guarding U.S. Medicare Against Rising Drug Costs (GUARD) Model, which proposes MFN-based rebates in Medicare Part D. The scope of these models and the impact that they could have on our products is unclear at this time.

If product liability or state consumer protection act lawsuits are brought against us, we may incur substantial liabilities and may be required to limit commercialization of our products.

We face an inherent risk of product liability as a result of our products and the clinical trials of our product candidates. For example, we may be sued if our products or product candidates allegedly cause injury or are found to be otherwise unsuitable during product testing, manufacturing, marketing or sale. Any such product liability claims may include allegations of defects in manufacturing, defects in design, a failure to warn of dangers inherent in the product candidate, negligence, strict liability and a breach of warranties. Claims may be brought against us by patients, clinical trial participants, or others using, administering or selling our products or product candidates, and could be asserted as product liability claims or under state consumer protection acts.

If we cannot successfully defend ourselves against product liability claims, we may incur substantial liabilities or be required to limit or cease the commercialization of our products. Even a successful defense would require significant financial and management resources. Regardless of the merits or eventual outcome, liability claims may result in:

- decreased demand for our products;
- injury to our reputation and significant negative media attention;
- withdrawal of clinical trial participants and potential termination of clinical trial sites or entire clinical programs;

- costs to defend the related litigation;
- a diversion of management's time and our resources;
- substantial monetary awards to trial participants or patients;
- product recalls, withdrawals or labeling, marketing or promotional restrictions;
- initiation of investigations and enforcement actions by regulators;
- significant negative financial impact;
- the inability to commercialize our products or product candidates; and
- a decline in our stock price.

We currently hold $10 million in product liability insurance coverage in the aggregate. We may need to increase our insurance coverage as we continue to commercialize PALSONIFY and expand clinical trials of our other product candidates. Insurance coverage is increasingly expensive. Our inability to obtain and retain sufficient product liability insurance at an acceptable cost to protect against potential product liability claims could prevent or inhibit the commercialization of our products and product candidates. Although we maintain such insurance, any claim that may be brought against us could result in a court judgment or settlement in an amount that is not covered, in whole or in part, by our insurance or that is in excess of the limits of our insurance coverage. Our insurance policies will also have various exclusions, and we may be subject to a product liability claim for which we have no coverage. We may have to pay any amounts awarded by a court or negotiated in a settlement that exceed our coverage limitations or that are not covered by our insurance, and we may not have, or be able to obtain, sufficient capital to pay such amounts, which could have a material adverse effect on our business, results of operations and financial condition.

We and any of our potential future collaborators will be required to report to regulatory authorities if any of our approved products cause or contribute to adverse medical events, and any failure to do so would result in sanctions that would materially harm our business.

The FDA and foreign regulatory authorities require that we and any of our potential future collaborators report certain information about adverse medical events if those products may have caused or contributed to those adverse events. The timing of our obligation to report would be triggered by the date we become aware of the adverse event as well as the nature of the event. We and any of our potential future collaborators or CROs may fail to report adverse events within the prescribed timeframe. If we or any of our potential future collaborators or CROs fail to comply with such reporting obligations, the FDA or a foreign regulatory authority could take action, including sanctions, criminal prosecution, the imposition of civil monetary penalties, seizure of our products or delay in approval or clearance of future products, which could have a material adverse effect on our business, results of operations and financial condition.

Our employees and independent contractors, including principal investigators, CROs, consultants, commercial partners and vendors may engage in misconduct or other improper activities, including noncompliance with regulatory standards and requirements.

We are exposed to the risk that our employees and independent contractors, including principal investigators, CROs, consultants, commercial partners and vendors may engage in misconduct or other improper or illegal activity. Misconduct by these parties could include intentional, reckless and/or negligent conduct or unauthorized activities that violate: (1) the laws and regulations of the FDA and other regulators and other similar regulatory requirements, including those laws that require the reporting of true, complete and accurate information to such authorities, manufacturing standards, (2) federal and state data privacy, security, fraud and abuse and other healthcare laws and regulations in the U.S. and abroad, or (3) laws that require the true, complete and accurate reporting of financial information or data. Activities subject to these laws also involve the improper use or misrepresentation of information obtained in the course of clinical trials, the creation of fraudulent data in our preclinical studies or clinical trials, or illegal misappropriation of drug product, which could result in regulatory sanctions and cause serious harm to our reputation. Sales, marketing and other business arrangements in the healthcare industry are also subject to extensive laws intended to prevent fraud, kickbacks, self-dealing and other abusive practices. These laws and regulations may restrict or prohibit a wide range of pricing, discounting, marketing and promotion, sales commission, customer incentive programs and other business arrangements. In addition, during the course of our operations our directors, executives, and employees may have access to material, nonpublic information regarding our business, our results of operations, or potential transactions we are considering. We may not be able to prevent a director, executive, or employee from trading in our common stock on the basis of, or while having access to, material, nonpublic information. It is not always possible to identify and deter misconduct by employees and other third parties, and the precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to be in compliance with such laws or regulations. In addition, we are subject to the risk that a person or government could allege such fraud or other misconduct, even if none occurred. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business and financial results, including, without limitation, the imposition of significant civil, criminal and administrative penalties,

damages, monetary fines, disgorgements, possible exclusion from participation in Medicare, Medicaid and other federal healthcare programs, individual imprisonment, contractual damages, reputational harm, diminished profits and future earnings, additional reporting requirements and oversight if we become subject to a corporate integrity agreement or similar agreement to resolve allegations of non-compliance with these laws, and curtailment of our operations, any of which could adversely affect our ability to operate our business and our results of operations.

We may not realize any benefits from our relationship with Radionetics.

We no longer hold a majority equity stake in Radionetics, and we do not control any of its key activities. Radionetics will continue to need additional capital to advance its pipeline, and our ownership interest may be further diluted in connection with future capital raising. In addition, our ability to receive milestone or royalty payments from Radionetics subject and pursuant to the terms of the Radionetics License will depend on Radionetics' ability to advance its pipeline through clinical development, regulatory approval and ultimately commercial sales, all of which will take significant time, will be subject to inherent risks in drug development and may be impacted by changes in regulatory requirements, healthcare reform measures and competitive dynamics. Further, the Radionetics nonpeptide therapeutics platform technology targeting the delivery of therapeutic radioisotopes is novel and unproven and may never lead to approved products of commercial value. As a result, we may never realize future value from our equity interest in Radionetics, the Radionetics License or research collaboration with Radionetics, which could have a material adverse effect on our financial condition and the trading price of our common stock.

The increasing use of social media and artificial intelligence-based platforms presents new risks and challenges.

Social media is increasingly being used to communicate about our products and product candidates, technologies and programs, and the diseases our product candidates are designed to treat. Social media practices in the biopharmaceutical industry continue to evolve and regulations relating to such use are not always clear. This evolution creates uncertainty and risk of noncompliance with regulations applicable to our business. For example, patients may use social media channels to comment on the effectiveness of a product or product candidate or to report an alleged adverse event. When such disclosures occur, there is a risk that we fail to monitor and comply with applicable adverse event reporting obligations or we may not be able to defend ourselves or the public's legitimate interests in the face of the political and market pressures generated by social media due to restrictions on what we may say about our product candidates. There is also a risk of inappropriate disclosure of sensitive information or negative or inaccurate posts or comments about us on any social networking website. In addition, our employees may knowingly or inadvertently make use of social media in ways that may not comply with our social media policy or other legal or contractual requirements, which may give rise to liability, lead to the loss of trade secrets or other intellectual property, or result in public exposure of personal data of our employees, clinical trial participants and others. If any of these events were to occur or we otherwise fail to comply with applicable regulations, we could incur liability, face overly restrictive regulatory actions or incur other harm to our business. Additionally, artificial intelligence, or AI, -based solutions are increasingly being used in the biotechnology and biopharmaceutical industries, and as with many developing technologies, presents risks and challenges to our business. We and our contractors or third parties on which we rely may use AI solutions, which may give rise to liability, cause the loss or inadvertent release of data or intellectual property, result in reputational harm, or lead to outcomes with unintended biases or other consequences. AI systems may produce incorrect, incomplete, misleading or non-reproducible outputs (including "hallucinations"), may incorporate biases, and may be difficult to validate, explain, audit or control. Errors or failures could adversely affect the integrity of our research, clinical trials, regulatory submissions, product quality, patient safety, timelines and costs, and could lead to regulatory scrutiny or enforcement. The misuse of AI solutions could also result in unauthorized access and use of personal data of our employees, clinical trial participants, collaborators or other third parties. The legal and regulatory landscape for AI is rapidly evolving in the U.S. and internationally (including in the European Union), and may require us to implement additional governance, documentation, validation, monitoring, cybersecurity and compliance measures and incur significant costs, or may limit or delay our ability to use AI in our operations. Any of these events could have a material adverse effect on our business, prospects, operating results, and financial condition and could adversely affect the price of our common stock.

Risks related to our intellectual property

Our success depends on our ability to protect our intellectual property and our proprietary technologies, and if we are unable to protect our intellectual property and technologies, our business will suffer.

Our commercial success depends in part on our ability to obtain and maintain intellectual property protection for our product and product candidates, proprietary technologies, and their uses, as well as our ability to operate without infringing the proprietary rights of others. We generally seek to protect our proprietary position by filing patent applications in the U.S. and abroad related to our product candidates, proprietary technologies and their uses that are important to our business. Our patent applications cannot be enforced against third parties practicing the technology claimed in such applications unless, and until, patents issue from such applications, and then only to the extent the issued claims cover the

technology. There can be no assurance that our patent applications will result in patents being issued or that issued patents will afford sufficient protection against competitors with similar technology, nor can there be any assurance that the patents issued will not be infringed, designed around, or invalidated by third parties. Even issued patents may later be found invalid or unenforceable or may be modified or revoked in proceedings instituted by third parties before various patent offices or in courts. The degree of future protection for our proprietary rights is uncertain. Only limited protection may be available and may not adequately protect our rights or permit us to gain or keep any competitive advantage. This failure to obtain effective intellectual property rights relating to our product candidates could have a material adverse effect on our financial condition and results of operations.

The patent positions of companies like ours are generally uncertain and involve complex legal and factual questions. No consistent policy regarding the scope of claims allowable in patents in the pharmaceutical and biotechnology space has emerged in the U.S. The relevant patent laws and their interpretation outside of the U.S. is also uncertain. Changes in either the patent laws or their interpretation in the U.S. and other countries may diminish our ability to protect our technology or product candidates and could affect the value of such intellectual property. In particular, our ability to stop third parties from making, using, selling, offering to sell or importing products that infringe our intellectual property will depend in part on our success in obtaining and enforcing patent claims that cover our technology, inventions and improvements. We cannot guarantee that patents will be granted with respect to any of our pending patent applications or with respect to any patent applications we may file in the future, nor can we be sure that any patents that may be granted to us in the future will be commercially useful in protecting our products, the methods of use or manufacture of those products. Moreover, even our issued patents do not guarantee us the right to practice our technology in relation to the commercialization of our products. Patent and other intellectual property rights in the pharmaceutical and biotechnology space are evolving and involve many risks and uncertainties. For example, third parties may have blocking patents that could be used to prevent us from commercializing our product candidates and practicing our proprietary technology, and our issued patents may be challenged, invalidated or circumvented, which could limit our ability to stop competitors from marketing related products or could limit the term of patent protection that otherwise may exist for our product candidates. In addition, the scope of the rights granted under any issued patents may not provide us with protection or competitive advantages against competitors with similar technology. Furthermore, our competitors may independently develop similar technologies that are outside the scope of the rights granted under any issued patents. For these reasons, we may face competition with respect to our product candidates even if our patent applications are granted.

The patent application process is subject to numerous risks and uncertainties, and there can be no assurance that we or any of our potential future collaborators will be successful in protecting our product candidates by obtaining and defending patents. These risks and uncertainties include but are not limited to the following:

- the USPTO and various foreign governmental patent agencies require compliance with a number of procedural, documentary, fee payment and other provisions during the patent process, the noncompliance with which can result in abandonment or lapse of a patent or patent application, and partial or complete loss of patent rights in the relevant jurisdiction;
- patent applications may not result in any patents being issued;
- patents may be challenged, invalidated, modified, revoked, circumvented, found to be unenforceable or otherwise may not provide any competitive advantage;
- our competitors, many of whom have substantially greater resources than we do and many of whom have made significant investments in competing technologies, may seek or may have already obtained patents that will limit, interfere with or eliminate our ability to make, use and sell our potential product candidates;
- there may be significant pressure on the U.S. government, other governmental authorities, and international governmental bodies to limit the scope of patent protection both inside and outside the U.S. for disease treatments that prove successful, as a matter of public policy regarding worldwide health concerns; and
- countries other than the U.S. may have patent laws less favorable to patentees than those upheld by U.S. courts, allowing foreign competitors a better opportunity to create, develop and market competing product candidates.

The patent prosecution process is also expensive and time-consuming, and we may not be able to file and prosecute all necessary or desirable patent applications at a reasonable cost or in a timely manner or in all jurisdictions where protection may be commercially advantageous. It is also possible that we will fail to identify patentable aspects of our research and development output before it is too late to obtain patent protection. In addition, although we enter into non-disclosure and confidentiality agreements with parties who have access to patentable aspects of our research and development output, such as our employees, outside scientific collaborators, CROs, third-party manufacturers, suppliers, contractors, consultants, advisors and other third parties, any of these parties may breach such agreements and disclose such output before a patent application is filed, thereby jeopardizing our ability to seek patent protection.

Given the amount of time required for the development, testing and regulatory review of new product candidates, patents protecting such candidates might expire before or shortly after such candidates are commercialized. As a result, our

intellectual property may not provide us with sufficient rights to exclude others from commercializing products similar or identical to ours, which could have a material adverse effect on our business and prospects.

If the scope of any patent protection we obtain is not sufficiently broad, or if we lose any of our patent protection, our ability to prevent our competitors from commercializing similar or identical product candidates would be material and adversely affected.

The patent position of biopharmaceutical companies is generally highly uncertain, involves complex legal and factual questions, and has been the subject of much litigation in recent years. As a result, the issuance, scope, validity, enforceability and commercial value of our patent rights are highly uncertain. Our pending and future patent applications may not result in patents being issued that adequately protect our product candidates or that effectively prevent others from commercializing competitive products or product candidates.

Moreover, the coverage claimed in a patent application can be significantly reduced before the patent is issued, and its scope can be reinterpreted after issuance. Even if patent applications we own currently or in the future issue as patents, they may not issue in a form that will provide us with any meaningful protection, prevent competitors or other third parties from competing with us, or otherwise provide us with any competitive advantage. Any issued patents that we own may be challenged or circumvented by third parties or may be narrowed or invalidated as a result of challenges by third parties. Consequently, we do not know whether our products and product candidates will be protectable or remain protected by valid and enforceable patents. Our competitors or other third parties may be able to circumvent our patents by developing similar or alternative technologies or products in a non-infringing manner which could materially adversely affect our business, financial condition, results of operations and prospects.

The issuance of a patent is not conclusive as to its inventorship, scope, validity or enforceability. Our patents may be challenged in the courts or patent offices in the U.S. and abroad and may be narrowed or invalidated as a result of challenges by third parties. We may be subject to a third-party pre-issuance submission of prior art to the USPTO, or become involved in opposition, derivation, revocation, reexamination, PGR, and IPR, or other similar proceedings challenging our owned patent rights. An adverse determination in any such submission, proceeding or litigation could reduce the scope of, or invalidate or render unenforceable, our patent rights, allow third parties to commercialize our products or product candidates and compete directly with us, without payment to us, or result in our inability to manufacture or commercialize products without infringing third-party patent rights. Moreover, our patents may become subject to post-grant challenge proceedings, such as oppositions in a foreign patent office, which challenge our priority of invention or other features of patentability with respect to our patents and patent applications. Such challenges may result in loss of patent rights, loss of exclusivity or patent claims being narrowed, invalidated or held unenforceable, which could limit our ability to stop others from using or commercializing similar or identical technology and products, or limit the duration of the patent protection of our products and product candidates. Such proceedings also may result in substantial cost and require significant time from our scientists and management, even if the eventual outcome is favorable to us. In addition, if the breadth or strength of protection provided by our patents and patent applications is threatened, regardless of the outcome, it could dissuade companies from collaborating with us to license, develop or commercialize current or future product candidates, which could have a material adverse effect on our business and prospects.

Some of our intellectual property has been discovered through government funded programs and thus may be subject to federal regulations such as "march-in" rights, certain reporting requirements and a preference for U.S.-based companies. Compliance with such regulations may limit our exclusive rights and limit our ability to contract with non-U.S. manufacturers.

Some of our intellectual property rights, including those covering the compounds in our lead programs (paltusotine and atumelnant), have been generated through the use of U.S. government funding provided from SBIR Grants awarded to us by the NDDK of the NIH, and are therefore subject to certain federal regulations. As a result, the U.S. government may have certain rights to intellectual property embodied in our current or future product candidates pursuant to the Bayh-Dole Act. These U.S. government rights include a non-exclusive, non-transferable, irrevocable worldwide license to use inventions for any governmental purpose. In addition, the U.S. government has the right, under certain limited circumstances, to require us to grant exclusive, partially exclusive, or non-exclusive licenses to any of these inventions to a third party if it determines that: (i) adequate steps have not been taken to commercialize the invention; (ii) government action is necessary to meet public health or safety needs; or (iii) government action is necessary to meet requirements for public use under federal regulations (also referred to as "march-in rights"). The U.S. government also has the right to take title to these inventions if we fail to disclose the invention to the government or fail to file an application to register the intellectual property within specified time limits. Intellectual property generated under a government funded program is also subject to certain reporting requirements, compliance with which may require us to expend substantial resources. In addition, the U.S. government requires that any products embodying any of these inventions or produced through the use of any of these inventions be manufactured substantially in the U.S. This preference for U.S. industry may be waived by the

federal agency that provided the funding if the owner or assignee of the intellectual property can show that reasonable but unsuccessful efforts have been made to grant licenses on similar terms to potential licensees that would be likely to manufacture substantially in the U.S. or that under the circumstances domestic manufacture is not commercially feasible. This preference for U.S. industry may limit our ability to contract with non-U.S. product manufacturers for products covered by such intellectual property. To the extent any of our future intellectual property is also generated through the use of U.S. government funding, the provisions of the Bayh-Dole Act may similarly apply.

We may be involved in lawsuits to protect or enforce our patents, which could be expensive, time consuming and unsuccessful. Further, our issued patents could be found invalid or unenforceable if challenged in court.

Competitors may infringe our intellectual property rights. To prevent infringement or unauthorized use, we may be required to file infringement claims, which can be expensive and time-consuming. In addition, in a patent infringement proceeding, a court may decide that a patent we own is not valid, is unenforceable and/or is not infringed. If we or any of our potential future collaborators were to initiate legal proceedings against a third party to enforce a patent directed at one of our product candidates, the defendant could counterclaim that our patent is invalid and/or unenforceable in whole or in part. In patent litigation in the U.S., defendant counterclaims alleging invalidity and/or unenforceability are commonplace. Grounds for a validity challenge include an alleged failure to meet any of several statutory requirements, including but not limited to lack of novelty, obviousness, written description or non-enablement. Grounds for an unenforceability assertion could include an allegation that someone connected with prosecution of the patent withheld relevant information from the USPTO or made a misleading statement during prosecution.

Third parties may also raise similar invalidity claims before the USPTO or patent offices abroad, even outside the context of litigation. Such mechanisms include re-examination, PGR, IPR, derivation proceedings, and equivalent proceedings in foreign jurisdictions (e.g., opposition proceedings). Such proceedings could result in the revocation of, cancellation of or amendment to our patents in such a way that they no longer cover our technology or platform, or any product candidates that we may develop. The outcome following legal assertions of invalidity and unenforceability is unpredictable. With respect to the validity question, for example, we cannot be certain that there is no invalidating prior art, of which we and the patent examiner were unaware during prosecution. There is also no assurance that there is not prior art of which we are aware, but which we do not believe affects the validity or enforceability of a claim in our patents and patent applications, which may, nonetheless, ultimately be found to affect the validity or enforceability of a patent claim. If a third party were to prevail on a legal assertion of invalidity or unenforceability, we would lose at least part, and perhaps all, of the patent protection on our product candidates or other intellectual property that we may develop. In addition, if the breadth or strength of protection provided by our patents and patent applications is threatened, it could dissuade companies from collaborating with us to license, develop or commercialize current or future product candidates. Such a loss of patent protection would have a material adverse impact on our business, financial condition, results of operations and prospects.

Even if resolved in our favor, litigation or other legal proceedings relating to our intellectual property rights may cause us to incur significant expenses and could distract our technical and management personnel from their normal responsibilities. Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation or other legal proceedings relating to our intellectual property rights, there is a risk that some of our confidential information could be compromised by disclosure during this type of litigation or other proceedings. In addition, there could be public announcements of the results of hearings, motions or other interim proceedings or developments and if securities analysts or investors perceive these results to be negative, it could have a substantial adverse effect on the price of our common stock. Such litigation or proceedings could substantially increase our operating losses and reduce the resources available for development activities or any future sales, marketing or distribution activities. We may not have sufficient financial or other resources to conduct such litigation or proceedings adequately. Some of our competitors may be able to sustain the costs of such litigation or proceedings more effectively than we can because of their greater financial resources. Uncertainties resulting from the initiation and continuation of patent litigation or other proceedings could compromise our ability to compete in the marketplace.

Intellectual property rights do not necessarily address all potential threats to our competitive advantage.

The degree of future protection afforded by our intellectual property rights is uncertain because intellectual property rights have limitations and may not adequately protect our business or permit us to maintain our competitive advantage. For example:

- others may be able to develop products that are similar to our products and product candidates but that are not covered by the claims of the patents that we own;
- we might not have been the first to make the inventions covered by the issued patents or patent application that we own;
- we might not have been the first to file patent applications covering certain of our inventions;

- others may independently develop similar or alternative technologies or duplicate any of our technologies without infringing our intellectual property rights;
- it is possible that our pending patent applications will not lead to issued patents;
- issued patents that we own may be held invalid or unenforceable, as a result of legal challenges by our competitors;
- our competitors might conduct research and development activities in countries where we do not have patent rights and then use the information learned from such activities to develop competitive products for sale in our major commercial markets;
- we may not develop additional proprietary technologies that are patentable; and
- the patents of others may have an adverse effect on our business.

Should any of these events occur, it could significantly harm our business, results of operations and prospects.

Our commercial success depends significantly on our ability to operate without infringing the patents and other proprietary rights of third parties. Claims by third parties that we infringe their proprietary rights may result in liability for damages or prevent or delay our developmental and commercialization efforts.

Our commercial success depends in part on avoiding infringement of the patents and proprietary rights of third parties. However, our research, development and commercialization activities may be subject to claims that we infringe or otherwise violate patents or other intellectual property rights owned or controlled by third parties. Other entities may have or obtain patents or proprietary rights that could limit our ability to make, use, sell, offer for sale or import our products and product candidates that may be approved in the future, or impair our competitive position. There is a substantial amount of litigation, both within and outside the U.S., involving patent and other intellectual property rights in the biopharmaceutical industry, including patent infringement lawsuits, oppositions, reexaminations, IPR proceedings and PGR proceedings before the USPTO and/or corresponding foreign patent offices. Numerous third-party U.S. and foreign issued patents and pending patent applications exist in the fields in which we are developing product candidates. There may be third-party patents or patent applications with claims to materials, formulations, methods of manufacture or methods for treatment related to the use or manufacture of our product candidates.

As the biopharmaceutical industry expands and more patents are issued, the risk increases that our products and product candidates may be subject to claims of infringement of the patent rights of third parties. Because patent applications are maintained as confidential for a certain period of time, until the relevant application is published, we may be unaware of third-party patents that may be infringed by commercialization of any of our products or product candidates, and we cannot be certain that we were the first to file a patent application related to any product, product candidate or technology. Moreover, because patent applications can take many years to issue, there may be currently pending patent applications that may later result in issued patents that our products or product candidates may infringe. In addition, identification of third-party patent rights that may be relevant to our technology is difficult because patent searching is imperfect due to differences in terminology among patents, incomplete databases and the difficulty in assessing the meaning of patent claims. There is also no assurance that there is not prior art of which we are aware, but which we do not believe is relevant to our business, which may, nonetheless, ultimately be found to limit our ability to make, use, sell, offer for sale or import our products that may be approved in the future, or impair our competitive position. In addition, third parties may obtain patents in the future and claim that use of our technologies infringes upon these patents. Any claims of patent infringement asserted by third parties would be time consuming and could:

- result in costly litigation that may cause negative publicity;
- divert the time and attention of our technical personnel and management;
- cause development delays;
- prevent us from commercializing any of our product candidates until the asserted patent expires or is held finally invalid or not infringed in a court of law;
- require us to develop non-infringing technology, which may not be possible on a cost-effective basis;
- subject us to significant liability to third parties; or
- require us to enter into royalty or licensing agreements, which may not be available on commercially reasonable terms, or at all, or which might be non-exclusive, which could result in our competitors gaining access to the same technology.

Although no third party has asserted a claim of patent infringement against us as of the date of this Annual Report on Form 10-K, others may hold proprietary rights that could prevent our product candidates from being marketed once approved. Any patent-related legal action against us claiming damages and seeking to enjoin commercial activities relating to our products or processes could subject us to potential liability for damages, including treble damages if we were determined to willfully infringe, and require us to obtain a license to manufacture or market our products and product candidates. Defense of these claims, regardless of their merit, would involve substantial litigation expense and would be a substantial diversion

of employee resources from our business. We cannot predict whether we would prevail in any such actions or that any license required under any of these patents would be made available on commercially acceptable terms, if at all. Moreover, even if we or our future strategic partners were able to obtain a license, the rights may be nonexclusive, which could result in our competitors gaining access to the same intellectual property. In addition, we cannot be certain that we could redesign our products or product candidates or processes to avoid infringement, if necessary. Accordingly, an adverse determination in a judicial or administrative proceeding, or the failure to obtain necessary licenses, could delay or prevent us from developing and commercializing our products or product candidates, which could harm our business, financial condition and operating results. In addition, intellectual property litigation, regardless of its outcome, may cause negative publicity and could prohibit us from marketing or otherwise commercializing our products, product candidates and technology.

Parties making claims against us may be able to sustain the costs of complex patent litigation more effectively than we can because they have substantially greater resources. Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation or administrative proceedings, there is a risk that some of our confidential information could be compromised by disclosure. In addition, any uncertainties resulting from the initiation and continuation of any litigation could have material adverse effect on our ability to raise additional funds or otherwise have a material adverse effect on our business, results of operations, financial condition and prospects.

Intellectual property litigation may lead to unfavorable publicity that harms our reputation and causes the market price of our common shares to decline.

During the course of any intellectual property litigation, there could be public announcements of the initiation of the litigation as well as results of hearings, rulings on motions, and other interim proceedings in the litigation. If securities analysts or investors regard these announcements as negative, the perceived value of our existing products, programs or intellectual property could be diminished. Accordingly, the market price of shares of our common stock may decline. Such announcements could also harm our reputation or the market for our future products, which could have a material adverse effect on our business.

Derivation proceedings may be necessary to determine priority of inventions, and an unfavorable outcome may require us to cease using the related technology or to attempt to license rights from the prevailing party.

Derivation proceedings provoked by third parties or brought by us or declared by the USPTO may be necessary to determine the priority of inventions with respect to our patents or patent applications. An unfavorable outcome could require us to cease using the related technology or to attempt to license rights to it from the prevailing party. Our business could be harmed if the prevailing party does not offer us a license on commercially reasonable terms. Our defense of derivation proceedings may fail and, even if successful, may result in substantial costs and distract our management and other employees. In addition, the uncertainties associated with such proceedings could have a material adverse effect on our ability to raise the funds necessary to continue our clinical trials, continue our research programs, license necessary technology from third parties or enter into development or manufacturing partnerships that would help us bring our product candidates to market.

Changes in U.S. patent law, or laws in other countries or jurisdictions, could diminish the value of patents in general, thereby impairing our ability to protect our products and product candidates.

As is the case with other pharmaceutical companies, our success is heavily dependent on intellectual property, particularly patents. Obtaining and enforcing patents in the pharmaceutical industry involve a high degree of technological and legal complexity. Therefore, obtaining and enforcing pharmaceutical patents is costly, time consuming and inherently uncertain. Changes in either the patent laws or in the interpretations of patent laws in the U.S. and other countries may diminish the value of our intellectual property and may increase the uncertainties and costs surrounding the prosecution of patent applications and the enforcement or defense of issued patents. We cannot predict the breadth of claims that may be allowed or enforced in our patents or in third-party patents. In addition, the U.S. Congress or other foreign legislative bodies may pass patent reform legislation that is unfavorable to us.

For example, the U.S. Supreme Court has ruled on several patent cases in recent years, either narrowing the scope of patent protection available in certain circumstances or weakening the rights of patent owners in certain situations. In addition to increasing uncertainty with regard to our ability to obtain patents in the future, this combination of events has created uncertainty with respect to the value of patents, once obtained. Depending on decisions by the U.S. Congress, the U.S. federal courts, the USPTO, or similar authorities in foreign jurisdictions, the laws and regulations governing patents could change in unpredictable ways that would weaken our ability to obtain new patents or to enforce our existing patents and patents we might obtain in the future. For example, the IRA passed by Congress authorizes the Secretary of the Department of HHS to negotiate prices directly with participating manufacturers for selected medicines covered by Medicare even if these medicines are protected by an existing patent. For small molecule medicines, the process begins seven years after initial approval by the FDA. While we do not believe that the IRA or its effects will impact our ability to obtain patents in

the near future, we cannot be certain whether it will affect our patent strategy in the long run. The FDA has announced and may further implement, policies to increase transparency by publicly releasing portions of CRLs issued to drug and biologic sponsors. While the FDA has stated that confidential information will be protected, it remains unclear how such disclosures will be implemented. Because CRLs often contain specific observations about study design, clinical endpoints, chemistry, manufacturing, and controls (CMC) data, or other proprietary information, any public release could unintentionally disclose information that competitors may use to infer proprietary aspects of our product candidates or platform technologies. This could compromise the confidentiality of our trade secrets and know-how or facilitate third-party efforts to design around or challenge the validity, enforceability, or scope of our patents, or accelerate the development of generics or biosimilars. If we are required to modify or limit the information shared with the FDA to mitigate such risks, it could increase costs, slow our regulatory interactions, or delay future product approval timelines.

We may be subject to claims challenging the inventorship or ownership of our patents and other intellectual property.

We may also be subject to claims that former employees or other third parties have an ownership interest in our patents or other intellectual property. Litigation may be necessary to defend against these and other claims challenging inventorship or ownership. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights. Such an outcome could have a material adverse effect on our business. Even if we are successful in defending against such claims, litigation could result in substantial costs and distraction to management and other employees.

Patent terms may be inadequate to protect our competitive position on our product candidates for an adequate amount of time.

Patents have a limited lifespan. In the U.S., if all maintenance fees are timely paid, the natural expiration of a patent is generally 20 years from its earliest U.S. non-provisional filing date. Various extensions may be available, but the life of a patent, and the protection it affords, is limited. Even if patents covering our product candidates are obtained, once the patent life has expired, we may be open to competition from competitive products. Given the amount of time required for the development, testing and regulatory review of new product candidates, patents protecting such candidates might expire before or shortly after such candidates are commercialized, thereby reducing the commercial advantage the patent provides. As a result, our potential revenue could be materially reduced, and our patent portfolio may not provide us with sufficient rights to exclude others from commercializing products similar or identical to ours.

If we do not obtain patent term extension for our product candidates, our business may be materially harmed.

Depending upon the timing, duration and specifics of FDA marketing approval of our product candidates, one or more of our U.S. patents may be eligible for limited patent term restoration under the Hatch-Waxman Amendments. The Hatch-Waxman Amendments permit a patent restoration term of up to five years as compensation for patent term lost during product development and the FDA regulatory review process. A maximum of one patent may be extended per FDA approved product as compensation for the patent term lost during the FDA regulatory review process. A patent term extension cannot extend the remaining term of a patent beyond a total of 14 years from the date of product approval and only those claims covering such approved drug product, a method for using it or a method for manufacturing it may be extended. Patent term extension may also be available in certain foreign countries upon regulatory approval of our product candidates. However, we may not be granted an extension because of, for example, failing to apply within applicable deadlines, failing to apply prior to expiration of relevant patents or otherwise failing to satisfy applicable requirements. Moreover, the applicable time period or the scope of patent protection afforded could be less than we request. If we are unable to obtain patent term extension or restoration or the term of any such extension is less than we request, our competitors may obtain approval of competing products following our patent expiration, and our revenue could be reduced, possibly materially. Further, if this occurs, our competitors may take advantage of our investment in development and trials by referencing our clinical and preclinical data and launch their product earlier than might otherwise be the case.

We may not be able to protect our intellectual property rights throughout the world.

Patents are of national or regional effect. Filing, prosecuting and defending patents in all countries throughout the world could be prohibitively expensive, and our intellectual property rights in some countries outside the U.S. can be less extensive than those in the U.S. In addition, the laws of some foreign countries do not protect intellectual property rights to the same extent as federal and state laws in the U.S. Consequently, we may not be able to prevent third parties from practicing our inventions in all countries outside the U.S. or from selling or importing products made using our inventions in and into the U.S. or other jurisdictions. Competitors may use our technologies in jurisdictions where we have not obtained patent protection to develop their own products and, further, may export otherwise infringing products to territories where we have patent protection, but enforcement is not as strong as that in the U.S. These products may compete with our product candidates, and our patents or other intellectual property rights may not be effective or sufficient to prevent them from competing.

Many companies have encountered significant problems in protecting and defending intellectual property rights in foreign jurisdictions. The legal systems of many foreign countries do not favor the enforcement of patents and other intellectual property protection, which could make it difficult for us to stop the infringement of our patents or marketing of competing products in violation of our proprietary rights. As an example, as of June 2023, European patent applications have the option, upon grant of a patent, of becoming a Unitary Patent, which is subject to the jurisdiction of the UPC. Patents granted before the implementation of the UPC have the option of opting out of the jurisdiction of the UPC and remaining as national patents in the UPC countries. Patents that remain under the jurisdiction of the UPC may be potentially vulnerable to a single UPC-based revocation challenge that, if successful, could invalidate the patent in all countries who ratified the Unitary Patent Court Agreement. The option of a Unitary Patent is a significant change in European patent practice. As the UPC is a new court system, there is only limited precedent for the court, increasing the uncertainty. Proceedings to enforce our patent rights in foreign jurisdictions could result in substantial costs and divert our efforts and attention from other aspects of our business, could put our patents at risk of being invalidated or interpreted narrowly and our patent applications at risk of not issuing and could provoke third parties to assert claims against us. We may not prevail in any lawsuits that we initiate, and the damages or other remedies awarded, if any, may not be commercially meaningful. Accordingly, our efforts to enforce our intellectual property rights around the world may be inadequate to obtain a significant commercial advantage from the intellectual property that we develop or license.

Many countries have compulsory licensing laws under which a patent owner may be compelled to grant licenses to third parties. In addition, many countries limit the enforceability of patents against government agencies or government contractors. In these countries, the patent owner may have limited remedies, which could materially diminish the value of such patent. If we are forced to grant a license to third parties with respect to any patents relevant to our business, our competitive position may be impaired, and our business, financial condition, results of operations and prospects may be adversely affected.

Further, the standards applied by the USPTO and foreign patent offices in granting patents are not always applied uniformly or predictably. As such, we do not know the degree of future protection that we will have on our product candidates, proprietary technologies, and their uses. While we will endeavor to try to protect our product candidates, proprietary technologies, and their uses, with intellectual property rights such as patents, as appropriate, the process of obtaining patents is time consuming, expensive, and unpredictable.

Further, geo-political actions in the U.S. and in foreign countries could increase the uncertainties and costs surrounding the prosecution or maintenance of our patent applications or those of any current or future licensors and the maintenance, enforcement or defense of our issued patents or those of any current or future licensors. For example, the U.S. and foreign government actions related to the war in Ukraine may limit or prevent filing, prosecution, and maintenance of patent applications in Russia. Government actions may also prevent maintenance of issued patents in Russia. These actions could result in abandonment or lapse of our patents or patent applications, resulting in partial or complete loss of patent rights in Russia. If such an event were to occur, it could have a material adverse effect on our business. In addition, a decree was adopted by the Russian government in March 2022, allowing Russian companies and individuals to exploit inventions owned by patentees that have citizenship or nationality in, are registered in, or have predominately primary place of business or profit-making activities in the U.S. and other countries that Russia has deemed unfriendly without consent or compensation. Consequently, we would not be able to prevent third parties from practicing our inventions in Russia or from selling or importing products made using our inventions in and into Russia. Further, many foreign countries could threaten to impose retaliatory measures that may adversely impact our intellectual property rights in those countries. For example, on March 14, 2025, Brazil enacted Law No. 15. 122/2025 (known as the “Economic Reciprocity Law”), which provides a framework that allows for the suspension of obligations related to foreign entities’ intellectual property rights. Additionally, changes in U.S. trade policy, including the imposition of new or increased tariffs as well as retaliatory measures by other countries, could adversely affect our patent strategy, such as where we choose to file, maintain, or enforce our patents. Also, if we are required to move our research or manufacturing activities to new regions, this may expose us to jurisdictions with weaker intellectual property enforcement, differing patent eligibility standards, or greater risk of compulsory licensing. These factors could compromise the protection or value of our proprietary technologies, including our core patents and related know-how. Accordingly, our competitive position may be impaired, and our business, financial condition, results of operations and prospects may be adversely affected.

Obtaining and maintaining our patent protection depends on compliance with various procedural, documentary, fee payment and other requirements imposed by regulations and governmental patent agencies, and our patent protection could be reduced or eliminated for non-compliance with these requirements.

Periodic maintenance fees, renewal fees, annuity fees and various other governmental fees on patents and/or applications will be due to the USPTO and various foreign patent offices at various points over the lifetime of our patents and/or applications. We have systems in place to remind us to pay these fees, and we rely on our outside patent annuity service to pay these fees when due. Additionally, the USPTO and various foreign patent offices, require compliance with a number of

procedural, documentary, fee payment and other similar provisions during the patent application process. We employ reputable law firms and other professionals to help us comply, and in many cases, an inadvertent lapse can be cured by payment of a late fee or by other means in accordance with rules applicable to the particular jurisdiction. However, there are situations in which noncompliance can result in abandonment or lapse of the patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. If such an event were to occur, it could have a material adverse effect on our business.

If our trademarks and trade names are not adequately protected, then we may not be able to build name recognition in our markets of interest and our business may be adversely affected.

Even though we have filed multiple trademark registration applications in the U.S., as well as jurisdictions outside the U.S., we cannot be certain that our registered or unregistered U.S. trademarks or trade names, or the corresponding trademarks or trade names registered in foreign territories, will not be challenged, infringed, circumvented or declared generic or determined to be infringing on other marks. We may not be able to protect our rights to these trademarks and trade names, which we need to build name recognition among potential partners or customers in our markets of interest. At times, competitors may adopt trade names or trademarks similar to ours, thereby impeding our ability to build brand identity and possibly leading to market confusion. In addition, there could be potential trade name or trademark infringement claims brought by owners of other registered trademarks or trademarks that incorporate variations of our registered or unregistered trademarks or trade names. Over the long term, if we are unable to establish name recognition based on our trademarks and trade names, then we may not be able to compete effectively, and our business may be adversely affected. Our efforts to enforce or protect our proprietary rights related to trademarks, trade secrets, domain names, copyrights or other intellectual property may be ineffective and could result in substantial costs and diversion of resources and could adversely affect our financial condition or results of operations.

If we are unable to protect the confidentiality of our trade secrets, our business and competitive position would be harmed.

In addition, we rely on the protection of our trade secrets, including unpatented know-how, technology and other proprietary information to maintain our competitive position. Although we have taken steps to protect our trade secrets and unpatented know-how, including entering into confidentiality agreements with third parties, and confidential information and inventions agreements with employees, consultants and advisors, we cannot provide any assurances that all such agreements have been duly executed, and any of these parties may breach the agreements and disclose our proprietary information, including our trade secrets, and we may not be able to obtain adequate remedies for such breaches. Enforcing a claim that a party illegally disclosed or misappropriated a trade secret is difficult, expensive and time-consuming, and the outcome is unpredictable. In addition, some courts inside and outside the U.S. are less willing or unwilling to protect trade secrets.

Moreover, third parties may still obtain this information or may come upon this or similar information independently, and we would have no right to prevent them from using that technology or information to compete with us. If any of these events occurs or if we otherwise lose protection for our trade secrets, the value of this information may be greatly reduced, and our competitive position would be harmed. If we do not apply for patent protection prior to such publication or if we cannot otherwise maintain the confidentiality of our proprietary technology and other confidential information, then our ability to obtain patent protection or to protect our trade secret information may be jeopardized.

We may be subject to claims that we have wrongfully hired an employee from a competitor or that we or our employees have wrongfully used or disclosed alleged confidential information or trade secrets of their former employers.

As is common in the pharmaceutical industry, in addition to our employees, we engage the services of consultants to assist us in the development of our product candidates. Many of these consultants, and many of our employees, were previously employed at, or may have previously provided or may be currently providing consulting services to, other pharmaceutical companies including our competitors or potential competitors. We may become subject to claims that we, our employees or a consultant inadvertently or otherwise used or disclosed trade secrets or other information proprietary to their former employers or their former or current clients. Litigation may be necessary to defend against these claims. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights or personnel, which could adversely affect our business. Even if we are successful in defending against these claims, litigation could result in substantial costs and be a distraction to our management team and other employees.

Risks related to our common stock

An active, liquid and orderly market for our common stock may not be maintained.

Our common stock began trading on the Nasdaq in 2018, and we can provide no assurance that we will be able to maintain an active trading market for our common stock. The lack of an active market may impair your ability to sell your shares at

the time you wish to sell them or at a price that you consider reasonable. An inactive market may also impair our ability to raise capital by selling shares and may impair our ability to acquire other businesses or technologies using our shares as consideration, which, in turn, could materially adversely affect our business.

The trading price of the shares of our common stock could be highly volatile, and purchasers of our common stock could incur substantial losses.

Our stock price has been and is likely to be volatile. The stock market in general and the market for stock of pharmaceutical companies in particular have experienced extreme volatility that has often been unrelated to the operating performance of particular companies. As a result of this volatility, investors may not be able to sell their common stock at or above the price at which they paid. The market price for our common stock may be influenced by those factors discussed in this "Risk Factors" section and many others, including:

- our ability to successfully commercialize PALSONIFY and any future product candidates;
- our ability to enroll subjects in our ongoing and planned clinical trials;
- results of our clinical trials and preclinical studies, and the results of trials of our competitors or those of other companies in our market sector;
- failure to meet or exceed drug development or financial projections we provide to the public or of the investment community;
- regulatory approval of our product candidates, or limitations to specific label indications or patient populations for its use, or changes or delays in the regulatory review process;
- regulatory or legal developments in the U.S. and foreign countries;
- changes in the structure of healthcare payment systems, especially in light of current reforms to the U.S. healthcare system;
- the success or failure of our efforts to acquire, license or develop additional product candidates;
- innovations or new products developed by us or our competitors;
- announcements by us or our competitors of significant acquisitions, strategic partnerships, joint ventures or capital commitments;
- manufacturing, supply or distribution delays or shortages;
- any changes to our relationship with any manufacturers, suppliers, future collaborators or other strategic partners;
- achievement of expected product sales and profitability;
- variations in our financial results or those of companies that are perceived to be similar to us;
- market conditions in the pharmaceutical sector and issuance of securities analysts' reports or recommendations;
- trading volume of our common stock;
- an inability to obtain additional funding;
- sales of our stock by us, insiders and stockholders;
- changes in accounting principles;
- general economic, industry and market conditions or other events or factors, many of which are beyond our control, such as the impact of any natural disasters, including related to climate change, or public health emergencies, inflation, interest rates, actual or anticipated bank failures, and international military and/or geopolitical conflicts, including between Russia and Ukraine and in the Middle East;
- additions or departures of key personnel; and
- intellectual property, product liability or other litigation by or against us.

In addition, in the past, stockholders have initiated class action lawsuits against pharmaceutical companies following periods of volatility in the market prices of these companies' stock. Such litigation, if instituted against us, could cause us to incur substantial costs and divert management's attention and resources, which could have a material adverse effect on our business, financial condition and results of operations.

Our executive officers, directors and principal stockholders, if they choose to act together, have the ability to control or significantly influence all matters submitted to stockholders for approval.

Our executive officers, directors and greater than 5% stockholders, in the aggregate, own approximately 59.4% of our outstanding common stock as of February 13, 2026. As a result, such persons, acting together, have the ability to control or significantly influence all matters submitted to our stockholders for approval, including the election and removal of directors and approval of any significant transaction, as well as our management and business affairs. This concentration of ownership may have the effect of delaying, deferring or preventing a change in control, impeding a merger, consolidation, takeover or other business combination involving us, or discouraging a potential acquiror from making a tender offer or otherwise attempting to obtain control of our business, even if such a transaction would benefit other stockholders.

We do not currently intend to pay dividends on our common stock, and, consequently, your ability to achieve a return on your investment will depend on appreciation, if any, in the price of our common stock.

We have never declared nor paid any cash dividend on our common stock. We currently anticipate that we will retain future earnings for the development, operation and expansion of our business and do not anticipate declaring or paying any cash dividends for the foreseeable future. In addition, the terms of any future debt agreements may preclude us from paying dividends. Any return to stockholders will therefore be limited to the appreciation of their stock. There is no guarantee that shares of our common stock will appreciate in value or even maintain the price at which stockholders have purchased their shares.

Sales of a substantial number of shares of our common stock by our existing stockholders in the public market could cause our stock price to fall.

Sales of a substantial number of shares of our common stock by our existing stockholders in the public market or the perception that these sales might occur could significantly reduce the market price of our common stock and impair our ability to raise adequate capital through the sale of additional equity securities.

Provisions in our charter documents and under Delaware law could discourage a takeover that stockholders may consider favorable and may lead to entrenchment of management.

Our amended and restated certificate of incorporation and amended and restated bylaws contain provisions that could significantly reduce the value of our shares to a potential acquiror or delay or prevent changes in control or changes in our management without the consent of our board of directors. The provisions in our charter documents include the following:

- a classified board of directors with three-year staggered terms, which may delay the ability of stockholders to change the membership of a majority of our board of directors;
- no cumulative voting in the election of directors, which limits the ability of minority stockholders to elect director candidates;
- the exclusive right of our board of directors, unless the board of directors grants such right to the stockholders, to elect a director to fill a vacancy created by the expansion of the board of directors or the resignation, death or removal of a director, which prevents stockholders from being able to fill vacancies on our board of directors;
- the required approval of at least 66-2/3% of the shares entitled to vote to remove a director for cause, and the prohibition on removal of directors without cause;
- the ability of our board of directors to authorize the issuance of shares of preferred stock and to determine the price and other terms of those shares, including preferences and voting rights, without stockholder approval, which could be used to significantly dilute the ownership of a hostile acquiror;
- the ability of our board of directors to alter our amended and restated bylaws without obtaining stockholder approval;
- the required approval of at least 66-2/3% of the shares entitled to vote to adopt, amend or repeal our amended and restated bylaws or repeal the provisions of our amended and restated certificate of incorporation regarding the election and removal of directors;
- a prohibition on stockholder action by written consent, which forces stockholder action to be taken at an annual or special meeting of our stockholders;
- an exclusive forum provision providing that the Court of Chancery of the State of Delaware will be the exclusive forum for certain actions and proceedings;
- the requirement that a special meeting of stockholders may be called only by the board of directors, which may delay the ability of our stockholders to force consideration of a proposal or to take action, including the removal of directors; and
- advance notice procedures that stockholders must comply with in order to nominate candidates to our board of directors or to propose matters to be acted upon at a stockholders' meeting, which may discourage or deter a potential acquiror from conducting a solicitation of proxies to elect the acquiror's own slate of directors or otherwise attempting to obtain control of us.

We are also subject to the anti-takeover provisions contained in Section 203 of the Delaware General Corporation Law. Under Section 203, a corporation may not, in general, engage in a business combination with any holder of 15% or more of its capital stock unless the holder has held the stock for three years or, among other exceptions, the board of directors has approved the transaction.

Our amended and restated certificate of incorporation and amended and restated bylaws provide that the Court of Chancery of the State of Delaware will be the exclusive forum for substantially all disputes between us and our stockholders, and our amended and restated bylaws provide that the federal district courts shall be the exclusive forum

for the resolution of any complaint asserting a cause of action arising under the Securities Act, which could limit our stockholders' ability to obtain a favorable judicial forum for disputes with us or our directors, officers or employees.

Our amended and restated certificate of incorporation and amended and restated bylaws provide that the Court of Chancery of the State of Delaware is the exclusive forum for any derivative action or proceeding brought on our behalf, any action asserting a breach of fiduciary duty, any action asserting a claim against us arising pursuant to the Delaware General Corporation Law, our amended and restated certificate of incorporation or our amended and restated bylaws, or any action asserting a claim against us that is governed by the internal affairs doctrine; provided, however, that this exclusive forum provision would not apply to suits brought to enforce any liability or duty created by the Securities Act or the Exchange Act or any other claim for which the federal courts have exclusive jurisdiction. Furthermore, our amended and restated bylaws also provide that unless we consent in writing to the selection of an alternative forum, the federal district courts of the U.S. shall be the exclusive forum for the resolution of any complaint asserting a cause of action arising under the Securities Act. These provisions may limit a stockholder's ability to bring a claim in a judicial forum that it finds favorable for disputes with us or our directors, officers or other employees, which may discourage such lawsuits against us and our directors, officers and other employees. Alternatively, if a court were to find this provision in our amended and restated certificate of incorporation and amended and restated bylaws to be inapplicable or unenforceable in an action, we may incur additional costs associated with resolving such action in other jurisdictions, which could adversely affect our business and financial condition.

Our ability to use net operating loss carryforwards and other tax attributes may be limited.

We have incurred substantial losses during our history, do not expect to become profitable in the near future, and may never achieve profitability. To the extent that we continue to incur net operating losses for tax purposes, or NOLs, such NOLs will carry forward to offset future taxable income (subject to limitations), if any, until such NOLs expire (if subject to expiration). At December 31, 2025, we had federal, state, and foreign NOL carryforwards of approximately $861.8 million, $258.1 million and $14.2 million, respectively. The federal loss carryforwards generated after 2017 of $855.4 million will carry forward indefinitely and can be used to offset up to 80% of future annual taxable income, while those loss carryforwards generated prior to 2018 begin expiring in 2035, unless previously utilized. $5.1 million of the state loss carryforwards will carry forward indefinitely. The other state loss carryforwards begin expiring in 2035, unless previously utilized. Of the Company's foreign loss carryforwards, $10.1 million begin expiring in 2032, unless previously utilized, and the remaining loss carryforwards do not expire. The Company also has federal and California R&D credit carryforwards and federal Orphan Drug Credits totaling $42.4 million, $21.5 million, and $34.5 million, respectively. The federal R&D credits begin to expire in 2030, unless previously utilized, while the state credits do not expire. The federal Orphan Drug credit carryforwards will begin to expire in 2040, unless previously utilized.

Our NOL carryforwards and other tax attributes (including tax credit carryforwards) are subject to review and possible adjustment by the Internal Revenue Service and state tax authorities. Moreover, in general, under Sections 382 and 383 of the Internal Revenue Code of 1986, as amended, or the Code, a corporation that undergoes an "ownership change" is subject to limitations on its ability to utilize its pre-ownership change NOL carryforwards or tax credit carryforwards to offset future taxable income or income tax liabilities, respectively. For these purposes, an ownership change generally occurs where the aggregate change in stock ownership of one or more stockholders or groups of stockholders owning at least 5% of a corporation's stock exceeds 50 percentage points over a rolling three-year period. Similar rules may apply under state or foreign tax laws. During 2020, we completed a study to assess whether any ownership changes within the meaning of Section 382 of the Code had occurred with respect to us for the time period prior to July 15, 2020. The study identified ownership changes during the fourth quarter of 2015, the first quarter of 2018 and the second quarter of 2020. We updated the study through December 31, 2025 and did not identify any additional ownership changes. These ownership changes have subjected, and will continue to subject, our NOLs and tax credits to an annual limitation on their utilization. However, our NOLs and tax credits are not expected to expire unused assuming we have taxable income or income tax liabilities in future periods. Although we do not expect these limitations to constrain utilization of our NOLs or tax credits, such limitations could result in the expiration of our NOLs or tax credits before they can be utilized and, if we are profitable, our future cash flows could be adversely affected due to our increased tax liability. In addition, future changes after December 31, 2025 in our stock ownership, could result in additional ownership changes and further annual limitations. We have recorded a full valuation allowance related to our NOL carryforwards and other deferred tax assets due to the uncertainty of the ultimate realization of the future benefits of those assets.

General risk factors

Raising additional capital may cause dilution to our stockholders, restrict our operations or require us to relinquish rights to our technologies or product candidates.

Until such time, if ever, as we can generate substantial product revenue, we expect to finance our cash needs primarily through equity offerings, such as public equity offerings and offerings under the Sales Agreement, and debt financings or

other capital sources, including collaborations, licenses and other similar arrangements. In addition, we may seek additional capital due to favorable market conditions or strategic considerations even if we believe we have sufficient funds for our current or near term operating plans. To the extent that we raise additional capital through the sale of equity or convertible debt securities, your ownership interest will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect your rights as a common stockholder. Debt financing and preferred equity financing, if available, may involve agreements that include covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends, which could have a material adverse effect on our business and operations, as well as the trading price of our commons stock.

In addition, if we raise funds through future collaborations, licenses and other similar arrangements, we may have to relinquish valuable rights to our technologies, future revenue streams, research programs or product candidates or grant licenses on terms that may not be favorable to us, which may have a material adverse effect on our business, prospects and may reduce the value of our common stock.

We may engage in strategic transactions that could impact our liquidity, increase our expenses and present significant distractions to our management.

From time to time, we have considered and we may in the future consider strategic and/or transformative transactions, such as acquisitions of companies, asset purchases and out-licensing or in-licensing of intellectual property, products or technologies. Additional potential transactions that we may consider in the future include a variety of business arrangements, including spin-offs, strategic partnerships, joint ventures, restructurings, divestitures, business combinations and investments. Any such transaction could be material and could disrupt our business or change our business profile, focus or strategy significantly. Any future transactions could increase our near and long-term expenditures, result in potentially dilutive issuances of our equity securities, including our common stock, or the incurrence of debt, contingent liabilities, amortization expenses or acquired in-process research and development expenses, any of which could affect our financial condition, liquidity and results of operations. Future transactions may also require us to obtain additional financing, which may not be available on favorable terms or at all. These transactions may never be successful and may require significant time and attention of management. In addition, the integration of any business that we may acquire in the future may disrupt our existing business and may be a complex, risky and costly endeavor for which we may never realize the full benefits and could delay our timelines or otherwise adversely affect our business. Accordingly, although there can be no assurance that we will undertake or successfully complete any transactions of the nature described above, any additional transactions that we do complete could have a material adverse effect on our business, results of operations, financial condition and prospects.

Our operating results may fluctuate significantly, which makes our future operating results difficult to predict and could cause our operating results to fall below expectations or any guidance we may provide.

Our quarterly and annual operating results may fluctuate significantly, which makes it difficult for us to predict our future operating results. These fluctuations may occur due to a variety of factors, many of which are outside of our control, including, but not limited to:

- the timing and cost of, and level of investment in, research, development, regulatory approval and commercialization activities relating to our products and product candidates, which may change from time to time;
- coverage and reimbursement policies with respect to our products and product candidates, if approved, and potential future drugs that compete with our products;
- the cost of manufacturing our products and product candidates, which may vary depending on the quantity of production and the terms of our agreements with third-party manufacturers;
- expenditures that we may incur to acquire, develop or commercialize additional products, product candidates and technologies;
- the level of demand for any approved products, which may vary significantly;
- future accounting pronouncements or changes in our accounting policies; and
- the timing and success or failure of preclinical studies or clinical trials for our product candidates or competing product candidates, or any other change in the competitive landscape of our industry, including consolidation among our competitors or partners.

The cumulative effects of these factors could result in large fluctuations and unpredictability in our quarterly and annual operating results. As a result, comparing our operating results on a period-to-period basis may not be meaningful. Investors should not rely on our past results as an indication of our future performance.

This variability and unpredictability could also result in our failing to meet the expectations of industry or financial analysts or investors for any period. If our revenue or operating results fall below the expectations of analysts or investors or below

any forecasts we may provide to the market, or if the forecasts we provide to the market are below the expectations of analysts or investors, the price of our common stock could decline substantially. Such a stock price decline could occur even when we have met any previously publicly stated revenue or earnings guidance we may provide.

We and any of our third-party manufacturers and suppliers may use potent chemical agents and hazardous materials, and any claims relating to improper handling, storage or disposal of these materials could be time consuming or costly.

We and any of our third-party manufacturers or suppliers will use biological materials, potent chemical agents and may use hazardous materials, including chemicals and biological agents and compounds that could be dangerous to human health and safety of the environment. Our operations and the operations of our third-party manufacturers and suppliers also produce hazardous waste products. Federal, state and local laws and regulations govern the use, generation, manufacture, storage, handling and disposal of these materials and wastes. Compliance with applicable environmental laws and regulations may be expensive, and current or future environmental laws and regulations may impair our product development efforts. In addition, we cannot eliminate the risk of accidental injury or contamination from these materials or wastes. We do not carry specific biological or hazardous waste insurance coverage, and our property, casualty and general liability insurance policies specifically exclude coverage for damages and fines arising from biological or hazardous waste exposure or contamination. In the event of contamination or injury, we could be held liable for damages or be penalized with fines in an amount exceeding our resources, and our clinical trials or regulatory approvals could be suspended.

Although we maintain workers' compensation insurance for certain costs and expenses we may incur due to injuries to our employees resulting from the use of hazardous materials or other work-related injuries, this insurance may not provide adequate coverage against potential liabilities. We do not maintain insurance for toxic tort claims that may be asserted against us in connection with our storage or disposal of biologic, hazardous or radioactive materials.

In addition, we may incur substantial costs in order to comply with current or future environmental, health and safety laws and regulations, which have tended to become more stringent over time. These current or future laws and regulations may impair our research, development or production efforts. Failure to comply with these laws and regulations also may result in substantial fines, penalties or other sanctions or liabilities, which could materially adversely affect our business, financial condition, results of operations and prospects.

Our information technology systems, or those of any of our CROs, manufacturers, other contractors or consultants or potential future collaborators, may fail or suffer security breaches, which could result in a material disruption of our product development programs.

We collect and maintain information in digital form that is necessary to conduct our business, and we are increasingly dependent on information technology systems, infrastructure, and data to operate our business. In the ordinary course of our business, we collect, store, process, and transmit large amounts of confidential information, including intellectual property, proprietary business information and personal information of third parties and our employees and contractors. It is critical that we do so in a secure manner to maintain the confidentiality and integrity of such confidential information.

Despite the implementation of security measures, our information technology systems and those of our current and any future CROs and other contractors, consultants and collaborators are vulnerable to attack, interruption and damage from computer viruses and malware (e.g. ransomware), malicious code, cyberattacks, hacking, phishing attacks, deep fakes and other social engineering schemes, attacks enhanced or facilitated by artificial intelligence, theft, misconduct or misuse by personnel or third parties, human error, fraud, denial or degradation of service attacks, credential harvesting, supply-chain attacks, technological malfunctions or failures, software bugs, data and information loss, sophisticated nation-state and nation-state-supported actors or unauthorized access or use by persons inside our organization, or persons with access to systems inside our organization. Cyber threats may be generic, or they may be custom crafted against our information systems. Our network and storage applications and those of our vendors may be subject to unauthorized access by hackers or information security breaches due to operator error, malfeasance or other system disruptions. Attacks upon information technology systems are increasing in their frequency, levels of persistence, sophistication and intensity, and are being conducted by sophisticated and organized groups and individuals, including nation states and nation-state-supported actors, with a wide range of motives and expertise. We may also face increased cybersecurity risks due to our reliance on internet technology and the number of our personnel who are working remotely, which may create additional opportunities for cybercriminals to exploit vulnerabilities. Furthermore, because the techniques used to obtain unauthorized access to, or to sabotage, systems change frequently and often are not recognized until launched against a target, we may be unable to anticipate these techniques or implement adequate preventative measures. We may also experience security breaches that may remain undetected for an extended period. Even if identified, we may be unable to adequately investigate or remediate incidents or breaches due to attackers increasingly using tools and techniques that are designed to circumvent controls, to avoid detection, and to remove or obfuscate forensic evidence.

We and certain of our service providers are from time to time subject to cyberattacks and security incidents, including several of the types of attacks noted above. While no prior attacks or incidents have had a material impact on us, if such an event were to occur and cause interruptions in our operations, it could result in a material disruption of our development programs and our business operations, whether due to a loss of our trade secrets or other similar disruptions. For example, the loss of clinical trial data from completed or future clinical trials could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. A data security breach could also lead to public exposure of personal information of our clinical trial patients, customers and others. We also rely on third parties to manufacture our product candidates, and similar events relating to their computer systems could also have a material adverse effect on our business. To the extent that any disruption or security breach were to result in a loss of, or damage to, our data or applications, or inappropriate disclosure of confidential or proprietary information, we could incur liability and the further development and commercialization of our products and product candidates could be delayed. If a disruption or security breach were to result in a loss of, or damage to, our data or systems, or inappropriate disclosure of confidential or proprietary or personal information, we could also incur liability, including litigation exposure, penalties and fines, expose us to significant expenses, including remediation expenses, and cause significant harm to our reputation and business. Reputational harm resulting from a significant cyber incident may cause unquantifiable damage to our established goodwill. Furthermore, federal, state and international laws and regulations can expose us to enforcement actions and investigations by regulatory authorities, and potentially result in regulatory penalties, fines and significant legal liability, if our information technology security efforts fail. The cyber threat landscape is continually changing, and we cannot guarantee that we will be able to adapt and change our cyber program to manage and mitigate associated risks. We maintain cyber liability insurance; however, this insurance may not be sufficient to cover the financial, legal, business or reputational losses that may result from an interruption or breach of our systems.

Business disruptions could seriously harm our future revenue and financial condition and increase our costs and expenses.

Our operations could be subject to terrorism, war, earthquakes, power shortages, telecommunications failures, water shortages, floods, hurricanes, typhoons, fires, extreme weather conditions, health epidemics and other natural or manmade disasters or business interruptions. We have not undertaken a systematic analysis of the potential consequences to our business and financial results from such disasters or other business interruptions, including those resulting from or amplified by climate change. We do not have a recovery plan for such disasters, and we are predominantly self-insured. Consequently, we do not carry sufficient insurance to compensate us for actual losses from interruption of our business that may occur, and any losses or damages incurred by us could harm our business. Additionally, we rely on third- party suppliers and manufacturers to produce our product candidates. Our ability to obtain clinical supplies of our product candidates could be disrupted if the operations of these suppliers and manufacturers were affected by a man-made or natural disaster or other business interruption, which could have a material adverse effect on our business. For example, the COVID-19 pandemic and government measures taken in response had a significant impact, both direct and indirect, on businesses and commerce, resulting in delays and interruptions in our drug manufacturing, nonclinical activities, clinical trials, review and approval timelines, and our discovery and development pipeline. A resurgence or the occurrence of another pandemic or other public health crisis could adversely affect our business, operations and financial results. In addition, our corporate headquarters is located in San Diego, California near major earthquake faults and fire zones, and the ultimate impact on us being consolidated in this geographical area is unknown. The occurrence of any of these business disruptions could seriously harm our operations and financial condition and increase our costs and expenses.

Unfavorable global economic conditions could adversely affect our business, financial condition and stock price.

The global credit and financial markets are currently, and have from time to time, experienced extreme volatility and disruptions, including severely diminished liquidity and credit availability, rising interest and inflation rates, fluctuations in currency exchange rates, declines in consumer confidence, declines in economic growth, supply chain shortages, increases in unemployment rates and uncertainty about economic stability. For example, the Federal Reserve recently raised interest rates multiple times in response to concerns about inflation and it may raise them again. Higher interest rates, coupled with reduced government spending and volatility in financial markets may increase economic uncertainty and affect consumer spending. Increased inflation rates can adversely affect us by increasing our costs, including labor and employee benefit costs. The financial markets and the global economy may also be adversely affected by the current or anticipated impact of military and/or geopolitical conflict, including the ongoing conflict between Russia and Ukraine, and in the Middle East, impact of a prolonged U.S. government shutdown, terrorism or other geopolitical events, with the potential to result in extreme volatility in the global capital markets and further global economic consequences, including the imposition of tariffs, disruptions of the global supply chain and energy markets. Sanctions imposed by the U.S. and other countries in response to such conflicts may also adversely impact the financial markets and the global economy, and any economic countermeasures by the affected countries or others could exacerbate market and economic instability.

A future recession or market correction or other significant geopolitical events could materially affect our business and the value of our common stock. Our general business strategy may be adversely affected by any such economic downturn, liquidity shortages, volatile business environment or continued unpredictable and unstable market conditions. If the current equity and credit markets deteriorate, including as a result of political unrest or war, or if adverse developments are experienced by financial institutions, it may cause short-term liquidity risk and also make any necessary debt or equity financing more difficult, more costly, more onerous with respect to financial and operating covenants and more dilutive. Failure to secure any necessary financing in a timely manner and on favorable terms could have a material adverse effect on our growth strategy, financial performance and stock price and could require us to delay or abandon clinical development plans. In addition, there is a risk that one or more of our current service providers, manufacturers and other partners may be adversely affected by the foregoing risks, which could directly affect our ability to attain our operating goals on schedule and on budget.

We are subject to U.S. and certain foreign export and import controls, sanctions, embargoes, anti-corruption laws and anti-money laundering laws and regulations. Compliance with these legal standards could impair our ability to compete in domestic and international markets. We can face criminal liability and other serious consequences for violations, which can harm our business.

We are subject to export and import control laws and regulations, including the U.S. Export Administration Regulations, U.S. Customs regulations, and various economic and trade sanctions regulations administered by the U.S. Treasury Department's Office of Foreign Assets Controls, and anti-corruption and anti-money laundering laws and regulations, including the U.S. Foreign Corrupt Practices Act of 1977, as amended, the U.S. domestic bribery statute contained in 18 U.S.C. § 201, the U.S. Travel Act, the USA PATRIOT Act, and other state and national anti-bribery and anti-money laundering laws in the countries in which we conduct activities. Anti-corruption laws are interpreted broadly and prohibit companies and their employees, agents, clinical research organizations, contractors and other collaborators and partners from authorizing, promising, offering, providing, soliciting or receiving, directly or indirectly, improper payments or anything else of value to recipients in the public or private sector.

We may engage third parties for clinical trials outside of the U.S., to sell our products abroad, and/or to obtain necessary permits, licenses, patent registrations and other regulatory approvals. We have direct or indirect interactions with officials and employees of government agencies or government-affiliated hospitals, universities and other organizations. We can be held liable for the corrupt or other illegal activities of our employees, agents, clinical research organizations, contractors and other collaborators and partners, even if we do not explicitly authorize or have actual knowledge of such activities. Any violations of the laws and regulations described above may result in substantial civil and criminal fines and penalties, imprisonment, the loss of export or import privileges, debarment, tax reassessments, breach of contract and fraud litigation, reputational harm and other consequences.

Furthermore, U.S. export control laws and economic sanctions prohibit the provision of certain products and services to countries, governments, and persons targeted by U.S. sanctions. U.S. sanctions that have been or may be imposed as a result of military conflicts in other countries may impact our ability to continue activities at clinical trial sites within regions covered by such sanctions. For example, as a result of the military conflict between Russia and Ukraine, the U.S. and its European allies announced the imposition of sanctions on certain industry sectors and parties in Russia and the regions of Crimea, Donetsk and Luhansk in Ukraine, as well as enhanced export controls on certain products and industries. These and any additional sanctions and export controls, as well as any economic countermeasures by the governments of Russia or other jurisdictions, could adversely impact our ability to continue activities at clinical trial sites within regions covered by such sanctions or directly or indirectly disrupt our supply chain. If we fail to comply with export and import regulations and such economic sanctions, penalties could be imposed, including fines and/or denial of certain export privileges.

If securities or industry analysts do not publish research or reports or publish unfavorable research or reports about our business, our stock price and trading volume could decline.

The trading market for our common stock depends in part on the research and reports that securities or industry analysts publish about us, our business, our market or our competitors. If securities or industry analysts do not continue coverage of our company, the trading price for our stock would be negatively impacted. In the event one or more of the analysts who covers us downgrades our stock, our stock price would likely decline. If one or more of these analysts ceases to cover us or fails to regularly publish reports on us, interest in our stock could decrease, which could cause our stock price or trading volume to decline.

The increasing focus and evolving expectations with respect to on environmental sustainability and social initiatives could increase our costs, harm our reputation and adversely impact our financial results.

There has been increasing public focus by investors, employees, environmental activists, the media, governmental and nongovernmental organizations and other stakeholders on a variety of environmental, social, and governance, or ESG, and other sustainability matters. We may experience pressure to make commitments relating to sustainability matters that affect us, including the design and implementation of specific risk mitigation strategic initiatives relating to sustainability. If we are not effective in addressing environmental, social and other sustainability matters affecting our business, or setting and meeting relevant sustainability goals, our reputation and financial results may suffer. In addition, we may experience increased costs in order to execute upon our sustainability goals and measure achievement of those goals, which could have an adverse impact on our business and financial condition.

Some investors may use third-party ESG ratings and reports to guide their investment strategies and, in some cases, may choose not to invest in us if they believe our ESG practices are inadequate. The criteria by which companies' ESG practices are assessed are evolving, which could result in greater expectations of us and cause us to undertake costly initiatives to satisfy such new criteria. Alternatively, if we elect not to or are unable to satisfy new criteria or do not meet the criteria of a specific third-party provider, some investors may conclude that our policies with respect to ESG are inadequate and choose not to invest in us.

In addition, this emphasis on environmental, social and other sustainability matters has resulted and may result in the adoption of new laws and regulations, including new reporting requirements. Additionally, in March 2024, the SEC adopted final rules that, among other matters, established a framework for reporting of climate-related risks. Subsequently, in April 2024, the SEC issued an order staying the new rules in response to legal challenges. To the extent the stay is lifted, rules imposing additional reporting obligations may become effective, and we could face increased costs and increased exposure to potential legal or regulatory action or claims. If we fail to comply with new laws, regulations or reporting requirements, our reputation and business could be adversely impacted.

In addition, in recent years "anti-ESG" efforts have gained momentum across the U.S., with several states and Congress having proposed or enacted "anti-ESG" policies, legislation, or initiatives or issued related legal opinions, and the current administration issued an executive order opposing diversity equity and inclusion, or DEI, initiatives in the private sector. Such anti-ESG and anti-DEI-related policies, legislation, initiatives, litigation, legal opinions, and scrutiny could result in us facing additional compliance obligations, becoming the subject of investigations and enforcement actions, or sustaining reputational harm.

Changes in tax laws may impact our financial condition and results of operations.

New income, sales, use or other tax laws, statutes, rules, regulations or ordinances could be enacted at any time, or interpreted, changed, modified or applied adversely to us, any of which could adversely affect our business operations and financial performance. We are currently unable to predict whether such changes will occur and, if so, the ultimate impact on our business. To the extent that such changes have a negative impact on us, our suppliers or our customers, including as a result of related uncertainty, these changes may materially and adversely impact our business, financial condition, results of operations and cash flows.

We could be subject to securities class action litigation.

In the past, securities class action litigation has often been brought against a company following a decline in the market price of its securities. This risk is especially relevant for us because pharmaceutical companies have experienced significant stock price volatility in recent years. If we face such litigation, it could result in substantial costs and a diversion of management's attention and resources, which could harm our business.

Item 1B. Unresolved Staff Comments

None.

Item 1C. Cybersecurity

Risk Management and Strategy

Cybersecurity represents a critical component of the Company's overall approach to risk management. The Company's cybersecurity policies, standards and practices follow recognized frameworks established by the National Institute of Standards and Technology, the International Organization for Standardization and other applicable industry standards. The Company generally approaches cybersecurity threats through a cross-functional, multilayered approach, with the specific goals of: (i) identifying, preventing and mitigating cybersecurity threats to the Company; (ii) preserving the confidentiality, security and availability of the information that we collect and store to use in our business; (iii) protecting the Company's intellectual property; (iv) maintaining the confidence of our patients, collaborators, health care providers, and prospective

and future customers, clients and business partners; and (v) providing appropriate public disclosure of cybersecurity risks and incidents when required.

The Company deploys systems safeguards that are designed to protect the Company's information systems from cybersecurity threats, including firewalls, intrusion prevention and detection systems, anti-malware functionality and access controls, which are evaluated and improved through ongoing vulnerability assessments and cybersecurity threat intelligence. In addition, the Company maintains a comprehensive, risk-based approach to identifying and overseeing cybersecurity risks presented by third parties, including vendors, service providers and other external users of the Company's systems, as well as the systems of third parties that could adversely impact our business in the event of a cybersecurity incident affecting those third-party systems.

The Company has established and maintains comprehensive incident response and recovery plans that fully address the Company's response to a cybersecurity incident and the recovery from a cybersecurity incident, and such plans are tested and evaluated on a regular basis. The Company regularly engages third parties to perform assessments on our cybersecurity measures, including information security maturity assessments, audits and independent reviews of our information security control environment and operating effectiveness. The results of such assessments, audits and reviews are reported to the Audit Committee and to the Board through the Audit Committee, and the Company adjusts its cybersecurity policies, standards, processes and practices as necessary based on the information provided by the assessments, audits and reviews.

Governance

The Board oversees the management of risks from cybersecurity threats through its Audit Committee, which receives periodic presentations and reports on cybersecurity risks and related mitigation efforts. The Audit Committee would also receive prompt and timely information regarding any cybersecurity incident that would meet the applicable established reporting thresholds, as well as ongoing updates regarding such incident until it has been addressed. At least twice each year, the Audit Committee discusses the Company's approach to cybersecurity risk management with the Company's CIO.

The Company's CIO oversees the Company's cybersecurity risk-management program and works with business leaders across the organization to identify and manage cybersecurity risks. Multidisciplinary teams throughout the Company are deployed to address cybersecurity threats and to respond to cybersecurity incidents in accordance with the Company's incident response and recovery plans. The Company's CIO has approximately 25 years of technology experience, including more than 20 years in the life sciences industry. He has served as Senior Vice President of Digital & Information Technology and Vice President of IT at multiple biopharmaceutical companies, with responsibility for emerging technologies, digital transformation, and infrastructure and security operations. He holds a Master of Business Administration and a Bachelor of Science in Information Systems and Operations Management from the University of Southern California. He also holds a Cyber Certificate from the National Association of Corporate Directors and a Master Certificate in IT Project Management from The George Washington University.

Risks from the cybersecurity threats we have faced to date have not materially affected, and we believe are not reasonably likely to affect, the Company, including its business strategy, results of operations or financial condition. However, due to evolving cybersecurity threats, we may not be able to protect all information systems, and integrating information systems as we acquire new businesses or expand our business may expose us to unexpected liabilities or increase our vulnerability. See "Risk Factors – General risk factors" for additional information about the risks to our business associated with a breach or compromise to our information technology systems.

Item 2. Properties

Our corporate headquarters consists of approximately 94,000 square feet of leased laboratory and office space in San Diego, California, which expires in April 2035.

We use our corporate headquarters to support our corporate, research and development, and commercial operations. We believe that our facilities are adequate to meet our current needs, and that suitable additional alternative spaces will be available in the future on commercially reasonable terms, if required.

Item 3. Legal Proceedings

We are not currently a party to any material legal proceedings. From time to time, we may be involved in legal proceedings or subject to claims incident to the ordinary course of business. Regardless of the outcome, such proceedings or claims can have an adverse impact on us because of defense and settlement costs, diversion of resources and other factors, and there can be no assurances that favorable outcomes will be obtained.

Item 4. Mine Safety Disclosures

None.

PART II

Item 5. Market for Registrant's Common Equity, Related Stockholder Matters and Issuer Purchases of Equity Securities

Market Information

Our common stock is listed on the Nasdaq Global Select Market under the ticker symbol "CRNX."

Holders of Common Stock

As of February 13, 2026, there were 7 registered holders of record of our common stock. This number was derived from our shareholder records and does not include beneficial owners of our common stock whose shares are held in the name of various dealers, clearing agencies, banks, brokers and other fiduciaries.

Dividend Policy

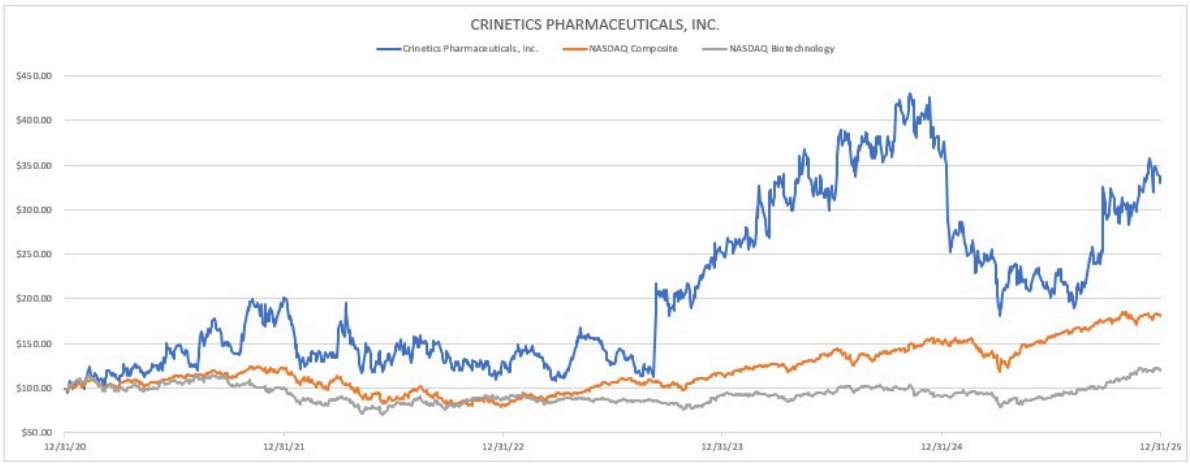
We have never declared or paid any cash dividends on our capital stock. We intend to retain future earnings, if any, to finance the operation of our business and do not anticipate paying any cash dividends in the foreseeable future. Any future determination related to dividend policy will be made at the discretion of our board of directors after considering our financial condition, results of operations, capital requirements, business prospects and other factors the board of directors deems relevant, and subject to the restrictions contained in any future financing instruments.

Securities Authorized for Issuance Under Equity Compensation Plans

See Item 12 of Part III of this Annual Report on Form 10-K for information about our equity compensation plans which is incorporated by reference herein.

Stock Performance Graph

The following stock performance graph compares our total stock return with the total return for (i) the Nasdaq Composite Index and the (ii) the Nasdaq Biotechnology Index for the five years ended December 31, 2025.



The figures represented below assume an investment of $100 in our common stock on December 31, 2020. The comparisons in the graph are not intended to forecast or be indicative of possible future performance of our common stock.

Company / Index	12/31/2020	12/31/2021	12/31/2022	12/31/2023	12/31/2024	12/31/2025
Crinetics Pharmaceuticals, Inc.	$ 100.00	$ 201.35	$ 129.70	$ 252.16	$ 362.37	$ 329.91
Nasdaq Biotechnology Index	$ 100.00	$ 99.37	$ 88.53	$ 91.84	$ 90.58	$ 119.92
Nasdaq Composite Index	$ 100.00	$ 121.39	$ 81.21	$ 116.47	$ 149.83	$ 180.33

Recent Sales of Unregistered Securities

None.

Issuer Repurchases of Equity Securities

None.

Item 6. [Reserved]

Item 7. Management's Discussion and Analysis of Financial Condition and Results of Operations

You should read the following discussion of our financial condition and results of operations in conjunction with all of the other information included in this Annual Report on Form 10-K, including the consolidated financial statements and the related notes thereto and "Risk Factors". This section of this Annual Report on Form 10-K generally discusses 2025 *and* 2024 *items and year-to-year comparisons between* 2025 *and* 2024. *Discussions of* 2023 *items and year-to-year comparisons between* 2024 *and* 2023 *that are not included in this Annual Report on Form 10-K can be found in the section entitled "Management's Discussion and Analysis of Financial Condition and Results of Operations" in Part II, Item 7 of the Company's Annual Report on Form 10-K for the year ended* December 31, 2024.

Overview

During 2025, we transitioned from a clinical-stage company to a commercial-stage company following the FDA approval and launch of PALSONIFY for the treatment of acromegaly in September 2025. As a result, our results of operations for the year ended December 31, 2025 reflect our initial period of commercial activity, including the generation of product revenue, commercialization-related costs, and continued investment in our research and development programs.

This management's discussion and analysis of financial condition and results of operations focuses on the key factors affecting our financial performance during this transition period, including initial product revenue net of gross-to-net adjustments, commercialization and operating expenses, collaboration and license revenue, and changes in liquidity and capital resources. Comparisons of our results for the year ended December 31, 2025 to prior periods should be viewed in the context of this shift to commercial operations.

We ended 2025 with a strong liquidity position, further strengthened by an underwritten public offering completed in January 2026, which provides capital to support our ongoing commercialization and development activities. See "Liquidity and Capital Resources" below.

As a newly commercial-stage company, we expect product revenue to increase as we continue to expand commercialization efforts for PALSONIFY. However, given the early stage of commercialization, we do not expect product revenue to be sufficient to offset operating expenses in the near term. We also expect operating expenses to increase as we continue to invest in commercialization, clinical development, and other research and development activities. Accordingly, we expect to continue to incur net losses for the foreseeable future.

Recent Developments

PALSONIFY

- On September 25, 2025, the FDA approved PALSONIFY as the first and only once-daily oral somatostatin receptor ligand for the treatment of adults with acromegaly who had an inadequate response to surgery and/or for whom surgery is not an option. We generated net product revenue of $5.4 million related to the PALSONIFY sales during the three months ended December 31, 2025.
- 2025 key metrics reflecting uptake from patients and healthcare providers, as well as payer feedback:
    - More than 200 enrollment forms received, including 22 from U.S.-based open-label extension participants.
    - Over 125 unique PALSONIFY prescribers, 50% of whom are from the community setting and 50% are from the pituitary treatment center setting.
    - Approximately half of newly filled bottles were reimbursed without need for Quickstart bridge supplies.
    - 12-month duration of most prior authorizations with approximately half of newly filled bottles reimbursed.

Paltusotine

- The first patient was enrolled in the Phase 3 study of paltusotine for CS in November 2025.
- In February 2026, the CHMP of the EMA adopted a positive opinion, recommending the marketing authorization of PALSONIFY for the medical treatment of adult patients with acromegaly. The CHMP opinion will be reviewed by the EC, consistent with a timeline for a potential decision in the first half of 2026.

Atumelnant

- In January 2025, we reported positive results from the first three cohorts of the Phase 2 TouCAHn open-label study of atumelnant in CAH. In January 2026, we provided an update, including data on the fourth cohort of the

Phase 2 TouCAHn study and data from the separate OLE study. Participants in all four cohorts were eligible to enroll in the OLE.

- In May 2025, we announced the design of our Phase 3 CALM-CAH study. The first participant in the CALM-CAH study was randomized in December 2025.
- In August 2025, we announced our pediatric trial design in CAH, BALANCE-CAH. BALANCE-CAH is designed as an operationally seamless Phase 2/3 study. The first participant in the BALANCE-CAH study was dosed in January 2026.
- We expect to initiate an operationally seamless Phase 2/3 study of atumelnant in ADCS (EQUILIBRIUM-ADCS) in the first half of 2026.

CRN09682

- In April 2025, we received IND clearance for CRN09682, the first candidate from the NDC platform. In November 2025, the first patient received CRN09682 in the dose escalation phase of a Phase 1/2 study.

For other product candidate updates, see "Business Overview."

Equity Offerings

On January 8, 2026, the Company completed an underwritten public offering of 8,763,000 shares of its common stock at a price to the public of $45.95 per share, which included 1,143,000 shares of common stock issued pursuant to the underwriters' option to purchase additional shares. Net proceeds from the offering were approximately $380.0 million, after underwriting discounts and commissions and other offering costs. After the completion of this public offering, the Company had approximately $1.4 billion in cash, cash equivalents, and investment securities.

Financial Operations Overview

During the year ended December 31, 2025, our financial results changed as we commercialized PALSONIFY following the FDA approval in September 2025 and the launch of PALSONIFY in the fourth quarter of 2025. As a result, our results now include product revenue for the first time, alongside collaboration and license revenue that historically represented our primary sources of revenue. Product revenue during 2025 reflects a partial year of commercialization and is subject to gross-to-net adjustments customary in the U.S. pharmaceutical market.

Our cost structure also evolved during 2025 as we incurred cost of product revenue and expanded our commercial infrastructure to support the launch of PALSONIFY. These changes resulted in increased operating expenses, including commercialization-related selling, general and administrative expenses, while we continued to invest in manufacturing readiness and supply chain activities necessary to support ongoing commercial operations.

While commercialization efforts expanded during 2025, research and development expenses increased as we progressed clinical development programs and supported earlier-stage research initiatives to advance our pipeline of product candidates.

Critical Accounting Estimates

This management's discussion and analysis of our financial condition and results of operations is based on our consolidated financial statements, which we have prepared in accordance with U.S. GAAP. The preparation of these consolidated financial statements requires us to make estimates and judgments that affect the reported amounts of assets, liabilities, revenue, and expenses and the disclosure of contingent assets and liabilities at the date of our consolidated financial statements. On an ongoing basis, we evaluate our estimates and judgments, including those listed below. We base our estimates on historical experience, known trends and events, information received from third parties and various other factors that we believe are reasonable under the circumstances at the time the estimates are made, the results of which form the basis for making judgments about the carrying values of assets and liabilities that are not readily apparent from other sources. Actual results may differ from these estimates under different assumptions or conditions. There were no material differences between estimates and actual results for the years presented in the accompanying consolidated financial statements.

Our significant accounting policies are described in more detail in Note 2 to the consolidated financial statements. We believe the following accounting estimates to be most critical to the preparation of our consolidated financial statements.

Accrued research and development expenses

As part of the process of preparing our consolidated financial statements, we are required to estimate our accrued expenses as of each balance sheet date. This process involves reviewing open contracts and purchase orders, communicating with

our personnel to identify services that have been performed on our behalf and estimating the level of service performed and the associated cost incurred for the service when we have not yet been invoiced or otherwise notified of the actual cost. We make estimates of our accrued expenses as of each balance sheet date based on facts and circumstances known to us at that time. We periodically confirm the accuracy of our estimates with the service providers and make adjustments if necessary. The significant estimates in our accrued research and development expenses include the costs incurred for services performed by our vendors in connection with research and development activities for which we have not yet been invoiced.

We base our expenses related to research and development activities on our estimates of the services received and efforts expended pursuant to quotes and contracts with vendors that conduct research and development on our behalf. The financial terms of these agreements are subject to negotiation, vary from contract to contract and may result in uneven payment flows. There may be instances in which payments made to our vendors will exceed the level of services provided and result in a prepayment of the research and development expense. In accruing service fees, we estimate the time period over which services will be performed and the level of effort to be expended in each period. If the actual timing of the performance of services or the level of effort varies from our estimate, we adjust the accrual or prepaid expense accordingly. Advance payments for goods and services that will be used in future research and development activities are expensed when the activity has been performed or when the goods have been received rather than when the payment is made.

Costs incurred under contracts with CROs that conduct and manage our clinical trials are also included in research and development expenses. The financial terms and activities of these agreements vary from contract to contract and may result in uneven expense levels. Clinical trial activities are accrued and expensed based on estimates of the period in which services and efforts are expended by CROs and other third parties. Estimates are determined by reviewing cost information provided by CROs, other third-party vendors and internal clinical personnel, and contractual arrangements with CROs and the scope of work to be performed. If the amounts that we are obligated to pay under our clinical trial agreements are modified (for instance, because of changes in the clinical trial protocol or scope of work to be performed), we adjust our accruals accordingly on a prospective basis. Revisions to contractual payment obligations are charged to expense in the period in which the facts that give rise to the revision become reasonably certain.

Although we do not expect our estimates to be materially different from amounts actually incurred, if our estimates of the status and timing of services performed differ from the actual status and timing of services performed, it could result in us reporting amounts that are too high or too low in any particular period. To date, there have been no material differences between our estimates of such expenses and the amounts actually incurred.

Revenue Recognition - Gross-to-Net Adjustments

Product revenue is recorded with each sale at wholesale acquisition cost, net of variable consideration and consideration payable to third parties associated with distribution of product. We utilize the expected value method when estimating the amount of variable consideration to include in the transaction price. Variable consideration is included in the transaction price only to the extent it is probable that a significant revenue reversal will not occur. These amounts include government rebates, chargebacks, distribution service fees, co-payment assistance and return reserve, which are collectively referred to as “Gross-to-Net Adjustments.” We must make significant judgments to determine the estimates for Gross-to-Net Adjustments. These estimates are reassessed each reporting period.

Results of Operations

Comparison of the years ended December 31, 2025 and 2024

The following table summarizes our results of operations for the years ended December 31, 2025 and 2024 (*in thousands)*:

	Year Ended December 31,		$	%
	2025	2024	Change	Change
Revenue:				
Product revenue, net	$ 5,420	$ —	$ 5,420	N/M
Collaboration and license revenue	2,276	1,039	1,237	119 %
Total revenue, net	7,696	1,039	6,657	641 %
Operating expenses:				
Cost of product revenue	1,076	—	1,076	N/M
Research and development	332,058	240,156	91,902	38 %
Selling, general and administrative	191,331	99,737	91,594	92 %
Total operating expenses	524,465	339,893	184,572	54 %
Loss from operations	(516,769)	(338,854)	(177,915)	53 %
Total other income, net	51,632	40,916	10,716	26 %
Loss before income taxes	(465,137)	(297,938)	(167,199)	56 %
Income tax expense	180	—	180	N/M
Loss before equity method investment	(465,317)	(297,938)	(167,379)	56 %
Loss on equity method investment	—	(470)	470	N/M
Net loss	$ (465,317)	$ (298,408)	$ (166,909)	56 %

N/M - percentage not meaningful

Revenue

Revenue during the year ended December 31, 2025 relates to PALSONIFY net product revenue and our partnership with SKK. We have recognized net product sales in the U.S. since the commercial launch of PALSONIFY in October 2025. We expect product revenue to increase in future periods as we continue with the commercial launch of PALSONIFY.

Revenue during the year ended December 31, 2024 relate to our partnership with SKK. The increase in collaboration and license revenue is attributable to the timing of the revenue recognition for the data exchange performance obligation under the SKK License.

Cost of product revenue

The following table summarizes our cost of product revenue for the year ended December 31, 2025 (*in thousands*):

	Year Ended December 31, 2025
Cost of product revenue:	
Commercial manufacturing readiness and supplier qualification costs	$ 826
Packaging, distribution, and other fulfillment costs	250
Total cost of product revenue	$ 1,076

Cost of product revenue for the year ended December 31, 2025 reflects commercial manufacturing readiness and supplier qualification costs incurred following regulatory approval of PALSONIFY and packaging, distribution, and other fulfillment-related costs. Product sales during 2025 were largely derived from inventory manufactured prior to regulatory approval of PALSONIFY, which had a zero cost basis as the related manufacturing costs were previously expensed as research and development in accordance with U.S. GAAP. As a result, cost of product revenue during this initial

commercialization period was not directly correlated with product revenue and does not reflect the Company's expected cost structure for future periods.

For the quarter and year ended December 31, 2025, the cost of product revenue would have increased by less than $0.1 million if we included previously expensed inventories.

Research and development expenses

Research and development expenses consist of costs incurred to support the discovery, preclinical development and clinical development of PALSONIFY and our product candidates. These expenses include personnel-related costs for employees engaged in research and development activities, external costs incurred under agreements with contract research organizations, investigative sites and consultants, costs to manufacture drug supply for preclinical studies and clinical trials, regulatory compliance costs, laboratory supplies, and allocated facility and overhead expenses.

Research and development expenses are expensed as incurred. Costs incurred to manufacture PALSONIFY prior to FDA approval were recorded as research and development expenses, resulting in zero-cost inventory upon approval.

Research and development expenses are driven by the scope, timing and progress of our clinical trials, including trial design, patient enrollment rates, trial duration, manufacturing requirements and regulatory activities. As a result, research and development spending may vary from period to period based on these factors and our strategic prioritization of programs.

We expect research and development expenses to increase as we continue to advance our pipeline and conduct ongoing and planned clinical and preclinical studies. However, the timing, duration and costs of these activities are subject to the inherent uncertainty associated with pharmaceutical research and development.

The following table summarizes our primary external and internal research and development expenses for the years ended December 31, 2025 and 2024 (*in thousands*):

	Year Ended December 31,		$	%
	2025	2024	Change	Change
External research and development expenses:				
Clinical trials	$ 64,741	$ 40,532	$ 24,209	60 %
Contract manufacturing	33,547	25,835	7,712	30 %
Preclinical studies	13,718	12,533	1,185	9 %
Outside services	46,399	33,817	12,582	37 %
Other external research and development	55	37	18	49 %
Total external research and development expenses	158,460	112,754	45,706	41 %
Internal expenses:				
Personnel expenses	102,677	70,772	31,905	45 %
Stock-based compensation	50,344	40,667	9,677	24 %
Depreciation and amortization	1,321	821	500	61 %
Facilities and related	10,602	10,480	122	1 %
Other internal research and development	8,654	4,662	3,992	86 %
Total internal research and development expenses	173,598	127,402	46,196	36 %
Total research and development expenses	$ 332,058	$ 240,156	$ 91,902	38 %

The increase in the majority of the categories above for the year ended December 31, 2025 since the corresponding prior year is as a result of the advancement of our clinical programs and preclinical portfolio.

The following table summarizes our research and development expenses by program for the years ended December 31, 2025 and 2024 (*in thousands*):

	Year Ended December 31,		$	%
	2025	2024	Change	Change
Paltusotine	$ 68,337	$ 51,229	$ 17,108	33 %
Atumelnant	48,131	24,524	23,607	96 %
Other research and development programs	33,322	26,010	7,312	28 %
Personnel expenses	102,677	70,772	31,905	45 %
Stock-based compensation	50,344	40,667	9,677	24 %
Depreciation and amortization	1,321	821	500	61 %
Other	27,926	26,133	1,793	7 %
Total research and development expenses	$ 332,058	$ 240,156	$ 91,902	38 %

The increase in research and development expenses of programs for the year ended December 31, 2025 as compared to the prior year was primarily due to clinical, manufacturing, and outside services costs related to paltusotine and atumelnant and increased investment across other research and development programs.

Selling, general and administrative expenses

Selling, general and administrative expenses consist of salaries and employee-related costs, including stock-based compensation, for personnel in commercial, finance, legal, human resources, information technology, and other corporate and administrative functions. Other significant components include sales and marketing expenses, facility-related costs, legal fees related to intellectual property and corporate matters, professional fees for accounting and consulting services, insurance costs, and commercial planning activities.

Selling, general and administrative expenses also include costs associated with operating as a public company, including audit, legal, regulatory and tax-related services required for compliance with SEC and exchange listing requirements, director and officer insurance premiums, corporate communications, investor relations activities, and corporate strategy and business development efforts.

We expect selling, general and administrative expenses to increase as we continue to support the commercialization of PALSONIFY, expand our commercial and administrative infrastructure, and advance our research and development activities, including the potential commercialization of additional product candidates if approved and expanding into additional markets beyond the U.S.

The following table summarizes our selling, general and administrative expenses for the years ended December 31, 2025 and 2024 (*in thousands*):

	Year Ended December 31,		$	%
	2025	2024	Change	Change
Other selling, general and administrative	$ 87,444	$ 36,769	$ 50,675	138 %
Personnel expenses	60,638	32,285	28,353	88 %
Stock-based compensation	40,680	28,719	11,961	42 %
Depreciation and amortization	2,569	1,964	605	31 %
Total selling, general and administrative expenses	$ 191,331	$ 99,737	$ 91,594	92 %

The increase in selling, general and administrative expenses for the year ended December 31, 2025 as compared to the prior year was primarily due to the increase in personnel expenses, including stock-based compensation, and professional services to support our growth, including the commercial launch of PALSONIFY.

Other income

Other income, net was $51.6 million and $40.9 million for the years ended December 31, 2025 and 2024, respectively. The increase was primarily due to income generated by our investment securities as a result of higher average invested balances and prevailing interest rates.

Loss on equity method investment

Loss on equity method investment was zero and $0.5 million for years ended December 31, 2025 and 2024, respectively. The loss recognized in 2024 reflected our share of Radionetics' net loss, which resulted in the investment asset being written down to zero.

Income taxes

Income tax expense was $0.2 million for the year ended December 31, 2025, compared to no income tax expense or benefit for the year ended December 31, 2024. The amount is not considered material.

Liquidity and Capital Resources

Our financial condition is summarized as follows (in thousands):

	December 31, 2025	December 31, 2024	$ Change	% Change
Cash and cash equivalents	$ 101,536	$ 264,545	$ (163,009)	(62)%
Investment securities	926,353	1,089,524	(163,171)	(15)%
Cash, cash equivalents and investment securities	$ 1,027,889	$ 1,354,069	$ (326,180)	(24)%
Working capital	$ 963,270	$ 1,315,704	$ (352,434)	(27)%
Accumulated deficit	$ (1,417,427)	$ (952,110)	$ (465,317)	49 %

We have funded our operations through equity financings, supplemented by license, collaboration and initial product revenue. As of December 31, 2025, we had cash, cash equivalents and investment securities of $1.0 billion. On January 8, 2026, the Company completed an underwritten public offering of 8,763,000 shares of its common stock for net proceeds of approximately $380.0 million, after underwriting discounts, commissions and other offering costs. Immediately after the completion of this offering, our cash, cash equivalents and investment securities was approximately $1.4 billion.

Based on our current and anticipated level of operations, we believe that our existing capital resources, together with income generated by our investment securities and product revenue, will be sufficient to satisfy our current and projected funding requirements for at least the next twelve months. However, our forecast of the period through which our financial resources will be adequate to support our operations is a forward-looking statement that involves risks and uncertainties, and actual results could vary materially. We have based this estimate on assumptions that may prove to be wrong, and we could use our capital resources sooner than we expect. Additionally, the process of testing product candidates in clinical trials is costly, and the timing of progress and expenses in these trials is uncertain.

Our future capital requirements will depend on many factors, including:

- the type, number, scope, progress, results, costs and timing of our preclinical studies and clinical trials of our product candidates which we are pursuing or may choose to pursue in the future;
- our ability to generate revenue through product sales of PALSONIFY and other potential product candidates once approved, if ever, and future licensing arrangements;
- the costs, timing and outcome of regulatory review of our product candidates;
- the costs associated with hiring additional personnel and consultants as our preclinical, clinical and commercial activities increase;
- the costs of and our ability to obtain clinical and commercial supplies for our current product candidates and any other product candidates we may identify and develop;
- the costs and timing of manufacturing for our product candidates, including commercial manufacturing;
- the costs of obtaining, maintaining and enforcing our patents and other intellectual property rights;
- our efforts to enhance operational systems and hire additional personnel to satisfy our obligations as a public company with a commercial pharmaceutical product, including enhanced internal controls over financial reporting, government price reporting and establishing and maintaining an effective compliance program;
- the costs and timing of establishing or securing sales and marketing capabilities for any additional product candidates that are approved;

- our ability to achieve sufficient market acceptance, adequate coverage and reimbursement from third-party payers and adequate market share and revenue for any approved products;
- the terms and timing of establishing and maintaining collaborations, licenses and other similar arrangements;
- costs associated with any products or technologies that we may in-license or acquire;
- the funding of any co-development arrangements we enter into; and
- general economic, industry and market conditions or other events or factors, many of which are beyond our control, such as the impact of any natural disasters, including related to climate change, or public health emergencies, inflation, interest rates, actual or anticipated bank failures, and international military or geopolitical conflicts, including between Russia and Ukraine and in the Middle East.

Until such time, if ever, as we can generate substantial product revenue to support our cost structure, we expect to finance our cash needs through our substantial existing capital resources, equity offerings, debt financings or other capital sources, including potential collaborations, licenses, and other similar arrangements. To the extent that we raise additional capital through the sale of equity or convertible debt securities, the ownership interest of our stockholders will be or could be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect the rights of our common stockholders. In addition, our ability to access financing on the terms we anticipate, or at all, may be impacted by volatility in global credit and financial markets, including as a result of inflation, rising interest rates, fluctuation in the value of the U.S. dollar and the effects, if any, of evolving international trade policies and government actions relating to tariffs. Debt financing and preferred equity financing, if available, may involve agreements that include covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures, or declaring dividends.

If we raise funds through collaborations, licenses, and other similar arrangements with third parties, we may have to relinquish valuable rights to our technologies, future revenue streams, research programs or product candidates or grant licenses on terms that may not be favorable to us and/or may reduce the value of our common stock. If we are unable to raise additional funds through equity or debt financings when needed, we may be required to delay, limit, reduce or terminate our product development or future commercialization efforts or grant rights to develop and market our product candidates even if we would otherwise prefer to develop and market such product candidates ourselves.

Equity Offerings

On March 1, 2024, we completed a private placement of 8,333,334 shares of its common stock at a price of $42.00 per share (the "Private Placement"). Net proceeds from the Private Placement were approximately $335.5 million, after offering costs of approximately $14.5 million.

On October 10, 2024, we completed an underwritten public offering of 11,500,000 shares of its common stock at a price to the public of $50.00 per share, which included 1,500,000 shares of common stock issued pursuant to the underwriters' option to purchase additional shares. Net proceeds from the offering were approximately $542.8 million, after underwriting discounts and commissions and other offering costs of approximately $32.2 million.

On January 8, 2026, we completed an underwritten public offering of 8,763,000 shares of its common stock at a price to the public of $45.95 per share, which included 1,143,000 shares of common stock issued pursuant to the underwriters' option to purchase additional shares. Net proceeds from the offering were approximately $380.0 million, after underwriting discounts and commissions and other offering costs.

ATM Offerings

In August 2019, we entered into the 2019 Sales Agreement with the Sales Agents, under which we could, from time to time, sell up to $150.0 million of shares of our common stock through the Sales Agents pursuant to the 2019 ATM Offering. The 2019 ATM Offering was terminated upon the filing of our Registration Statement on Form S-3ASR on June 21, 2024.

On June 21, 2024, we entered the 2024 Sales Agreement with the Sales Agents, under which we may, from time to time, sell up to $350.0 million of shares of our common stock through the Sales Agents pursuant to the 2024 ATM Offering. We are not obligated to, and we cannot provide any assurances that we will continue to, make any sales of the shares under the 2024 Sales Agreement. The 2024 Sales Agreement may be terminated by either Sales Agent (with respect to itself) or us at any time upon 10 days’ notice to the other parties, or by either Sales Agent, with respect to itself, at any time in certain circumstances, including the occurrence of a material adverse change. We will pay the Sales Agents a commission for their services in acting as agent in the sale of common stock in an amount equal to 3% of the gross sales price per share sold.

During the year ended December 31, 2024, the Company issued 1,223,775 shares of common stock for net proceeds of approximately $43.4 million and 928,912 shares of common stock for net proceeds of approximately $48.3 million, pursuant to the 2019 ATM Offering and the 2024 ATM Offering, respectively.

During the three months and year ended December 31, 2025 and the three months ended December 31, 2024, no shares of common stock were sold pursuant to the 2024 Sales Agreement.

Cash Flows

We have incurred cumulative net losses and negative cash flows from operations since our inception and expect to continue to incur net losses for the foreseeable future. As of December 31, 2025, we had an accumulated deficit of $1.4 billion and cash, cash equivalents and investment securities of $1.0 billion.

The following table provides information regarding our cash flows for the years ended December 31, 2025 and 2024 (*in thousands*):

	Year Ended December 31,		$	%
	2025	2024	Change	Change
Net cash used in operating activities	$ (377,922)	$ (230,194)	$ (147,728)	64 %
Net cash provided by (used in) investing activities	173,908	(574,817)	748,725	(130)%
Net cash provided by financing activities	40,611	1,014,659	(974,048)	(96)%
Net change in cash, cash equivalents and restricted cash	$ (163,403)	$ 209,648	$ (373,051)	(178)%

Cash Flows from Operating Activities

Cash used in operating activities is driven by personnel costs; clinical, manufacturing, and facility expenses; sales and marketing activities; and general and administrative support, partially offset by revenue generated from net product sales of PALSONIFY and our collaboration and license revenue. Our cash flows from operating activities will continue to be affected principally by our working capital requirements and the extent to which we increase spending on personnel, commercial activities, and research and development as our business grows.

The year-over-year net increase in cash used in operating activities is driven by expenditures related to supporting the Company's commercial growth, the advancement of our clinical programs, and the progression of our preclinical portfolio.

Cash Flows from Investing Activities

Cash flows from investing activities are driven by fluctuations in the timing of purchases and maturities of investments and, to a lesser extent, purchases of property and equipment. The year-over-year change in cash flows from investing activities is mainly attributable to differences in the mix and timing of investment purchases and maturities.

Cash Flows from Financing Activities

Net cash provided by financing activities consists of net proceeds from the sale of common stock, exercises of stock options, and shares issued under the ESPP. The year-over-year decrease in cash provided by financing activities is attributable to the net proceeds received from the sale of common stock in 2024, compared to none in 2025, as well as a net decrease in proceeds from stock option exercises and shares issued under the ESPP.

Common Stock and Common Stock Equivalents

As of February 13, 2026, outstanding shares of common stock were 104.7 million, outstanding stock options were 13.3 million, unvested restricted stock units were 2.3 million, and shares expected to be purchased under the ESPP, were 0.7 million.

Item 7A. Quantitative and Qualitative Disclosures about Market Risk

Interest Rate Risk

Our cash, cash equivalents and investment securities consist of cash held in readily available checking and money market accounts as well as short-term debt securities. We are exposed to market risk related to fluctuations in interest rates and market prices. Our primary exposure to market risk is interest rate sensitivity, which is affected by changes in the general level of U.S. interest rates. However, because of the short-term nature of the instruments in our portfolio, a sudden hypothetical 10% change in market interest rates would not be expected to have a material impact on our financial condition or results of operations.

Foreign Currency

We conduct a portion of our business in currencies other than our U.S. dollar functional currency. These transactions give rise to cash flows and monetary assets and liabilities that are denominated in currencies other than the U.S. dollar; the value of these amounts are exposed to changes in currency exchange rates from the time the transactions are originated until the time the cash settlement is converted into U.S. dollars.

We contract with vendors, CROs and investigational sites in several foreign countries, including countries in South America, Europe and the Asia Pacific. As such, we have exposure to fluctuations in foreign currency rates in connection with these agreements. We do not hedge our foreign currency exchange rate risk. Additionally, our subsidiaries expose us to foreign currency exchange risk. We believe this exposure to be immaterial and, to date, we have not incurred any material adverse effects from foreign currency changes on these contracts. As of December 31, 2025, the impact of a theoretical 10% change in the exchange rate would not result in a material gain or loss.

Item 8. Financial Statements and Supplementary Data

Our consolidated financial statements and the report of our independent registered accounting firm required pursuant to this item are incorporated by reference herein from the applicable information included in Item 15 of this Report and are presented beginning on page F-1.

Item 9. Changes in and Disagreements with Accountants on Accounting and Financial Disclosure

None.

Item 9A. Controls and Procedures

Evaluation of Disclosure Controls and Procedures

We maintain disclosure controls and procedures that are designed to ensure that information required to be disclosed in our Exchange Act reports is recorded, processed, summarized and reported within the time periods specified in the SEC's rules and forms, and that such information is accumulated and communicated to our management, including our chief executive officer and chief financial officer, as appropriate, to allow for timely decisions regarding required disclosure. In designing and evaluating the disclosure controls and procedures, management recognizes that any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving the desired control objectives, and management is required to apply its judgment in evaluating the cost-benefit relationship of possible controls and procedures. In addition, the design of any system of controls also is based in part upon certain assumptions about the likelihood of future events, and there can be no assurance that any design will succeed in achieving its stated goals under all potential future conditions; over time, control may become inadequate because of changes in conditions, or the degree of compliance with policies or procedures may deteriorate. Because of the inherent limitations in a cost-effective control system, misstatements due to error or fraud may occur and not be detected.

As required by SEC Rule 13a-15(b), we carried out an evaluation, under the supervision and with the participation of our management, including our chief executive officer and chief financial officer, of the effectiveness of the design and operation of our disclosure controls and procedures as of the end of the period covered by this Report. Based on the foregoing, our chief executive officer and chief financial officer concluded that our disclosure controls and procedures were effective as of December 31, 2025 at the reasonable assurance level.

Changes in Internal Control over Financial Reporting

During the quarter ended December 31, 2025, there have been no changes in our internal control over financial reporting that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

Management's Annual Report on Internal Control over Financial Reporting.

Our management is responsible for establishing and maintaining adequate internal control over financial reporting, as such term is defined in Rules 13a-15(f) and 15d-15(f) of the Exchange Act. Internal control over financial reporting is a process designed under the supervision and with the participation of our management, including our principal executive officer and principal financial officer, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with GAAP. Our internal control over financial reporting includes those policies and procedures that: (i) pertain to the maintenance of records that in reasonable detail accurately and fairly reflect the transactions and dispositions of our assets, (ii) provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with GAAP, and that our receipts and expenditures are being made only in accordance with authorizations of our management and directors, and (iii) provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use or disposition of our assets that could have a material effect on our financial statements. Because of its inherent limitations, internal controls

over financial reporting may not prevent or detect all misstatements. Therefore, even those systems determined to be effective can provide only reasonable assurance with respect to financial statement preparation and presentation.

As of December 31, 2025, our management assessed the effectiveness of our internal control over financial reporting using the criteria set forth by the Committee of Sponsoring Organizations of the Treadway Commission in Internal Control-Integrated Framework (2013). Based on this assessment, our management concluded that, as of December 31, 2025, our internal control over financial reporting was effective based on those criteria.

BDO USA, P.C., the independent registered public accounting firm that audited the consolidated financial statements included in this Annual Report on Form 10-K, was engaged to attest to and report on the effectiveness of the Company's internal control over financial reporting as of December 31, 2025, as stated in its report below.

Report of Independent Registered Public Accounting Firm

Stockholders and Board of Directors
Crinetics Pharmaceuticals, Inc.
San Diego, California

Opinion on Internal Control over Financial Reporting

We have audited Crinetics Pharmaceuticals, Inc.'s (the "Company's") internal control over financial reporting as of December 31, 2025, based on criteria established in *Internal Control – Integrated Framework (2013)* issued by the Committee of Sponsoring Organizations of the Treadway Commission (the "COSO criteria"). In our opinion, the Company maintained, in all material respects, effective internal control over financial reporting as of December 31, 2025, based on the COSO criteria.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States) ("PCAOB"), the consolidated balance sheets of the Company as of December 31, 2025 and 2024, the related consolidated statements of operations and comprehensive loss, stockholders' equity, and cash flows for each of the three years in the period ended December 31, 2025, and the related notes and our report dated February 26, 2026, expressed an unqualified opinion thereon.

Basis for Opinion

The Company's management is responsible for maintaining effective internal control over financial reporting and for its assessment of the effectiveness of internal control over financial reporting, included in the accompanying "Item 9A, Management's Annual Report on Internal Control over Financial Reporting". Our responsibility is to express an opinion on the Company's internal control over financial reporting based on our audit. We are a public accounting firm registered with the PCAOB and are required to be independent with respect to the Company in accordance with U.S. federal securities laws and the applicable rules and regulations of the Securities and Exchange Commission and the PCAOB.

We conducted our audit of internal control over financial reporting in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether effective internal control over financial reporting was maintained in all material respects. Our audit included obtaining an understanding of internal control over financial reporting, assessing the risk that a material weakness exists, and testing and evaluating the design and operating effectiveness of internal control based on the assessed risk. Our audit also included performing such other procedures as we considered necessary in the circumstances. We believe that our audit provides a reasonable basis for our opinion.

Definition and Limitations of Internal Control over Financial Reporting

A company's internal control over financial reporting is a process designed to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles. A company's internal control over financial reporting includes those policies and procedures that (1) pertain to the maintenance of records that, in reasonable detail, accurately and fairly reflect the transactions and dispositions of the assets of the company; (2) provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with generally accepted accounting principles, and that receipts and expenditures of the company are being made only in accordance with authorizations of management and directors of the company; and (3) provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use, or disposition of the company's assets that could have a material effect on the financial statements.

Because of its inherent limitations, internal control over financial reporting may not prevent or detect misstatements. Also, projections of any evaluation of effectiveness to future periods are subject to the risk that controls may become inadequate because of changes in conditions, or that the degree of compliance with the policies or procedures may deteriorate.

/s/ BDO USA, P.C.

San Diego, California

February 26, 2026

Item 9B. Other Information

Rule 10b5-1 Trading Plans

During the three months ended December 31, 2025, the following members of our Board of Directors and/or officers adopted, modified, or terminated a trading arrangement that is intended to satisfy the affirmative defense conditions of Rule 10b5-1(c):

Name	Title of Director or Officer	Action	Date of Action	Duration of Plan	Total Shares of Common Stock to be Sold
Scott Struthers	Chief Executive Officer	Termination of 10b5-1 Plan	12/1/2025	August 30, 2024 - December 1, 2025	Up to 75,000
Matthew Fust	Director	Termination of 10b5-1 Plan	12/31/2025	December 3, 2024 - December 31, 2025	Up to 18,092
Tobin Schilke	Chief Financial Officer	Adoption of 10b5-1 plan	11/10/2025	November 10, 2025 - November 10, 2026	Up to 6,762
Stephanie Okey	Director	Adoption of 10b5-1 plan	11/19/2025	November 19, 2025 - February 15, 2027	Up to 37,900
Rogerio Vivaldi Coelho	Director	Adoption of 10b5-1 plan	12/11/2025	December 11, 2025 - March 15, 2027	Up to 11,000
Jeff Knight	Chief Operating Officer	Adoption of 10b5-1 plan	12/12/2025	December 12, 2025 - March 19, 2027	Up to 266,214

Item 9C. Disclosure Regarding Foreign Jurisdictions that Prevent Inspections

Not applicable.

PART III

Item 10. Directors, Executive Officers and Corporate Governance.

Information required by this item will be contained in our definitive proxy statement to be filed with the Securities and Exchange Commission in connection with our 2026 Annual Meeting of Stockholders, or the Definitive Proxy Statement, which is expected to be filed not later than 120 days after the end of our fiscal year ended December 31, 2025, under the headings "Election of Directors," "Corporate Governance," "Our Executive Officers," and, if applicable, "Delinquent Section 16(a) Reports," and is incorporated herein by reference.

Code of Business Conduct and Ethics

We have adopted a Code of Business Conduct and Ethics that applies to our officers, directors and employees, which is available on our website at www.crinetics.com. The Code of Business Conduct and Ethics contains general guidelines for conducting the business of our company consistent with the highest standards of business ethics and is intended to qualify as a "code of ethics" within the meaning of Section 406 of the Sarbanes-Oxley Act of 2002 and Item 406 of Regulation S-K. In addition, we intend to promptly disclose (i) the nature of any amendment to our Code of Business Conduct and Ethics that applies to our principal executive officer, principal financial officer, principal accounting officer or controller or persons performing similar functions and (ii) the nature of any waiver, including an implicit waiver, from a provision of our code of ethics that is granted to one of these specified officers, the name of such person who is granted the waiver and the date of the waiver on our website in the future.

Item 11. Executive Compensation.

Information required by this item will be contained in our Definitive Proxy Statement under the heading "Executive Compensation and Other Information," and is incorporated herein by reference.

Item 12. Security Ownership of Certain Beneficial Owners and Management and Related Stockholder Matters.

Information required by this item will be contained in our Definitive Proxy Statement under the heading "Security Ownership of Certain Beneficial Owners and Management," and is incorporated herein by reference.

Information required by Item 201(d) of Regulation S-K will be contained in our Definitive Proxy Statement under the heading "Executive Compensation and Other Information" and is incorporated herein by reference.

Item 13. Certain Relationships and Related Transactions, and Director Independence.

Information required by this item will be contained in our Definitive Proxy Statement under the headings "Certain Relationships and Related Person Transactions," "Board Independence" and "Committees of the Board of Directors" and is incorporated herein by reference.

Item 14. Principal Accounting Fees and Services.

Information required by this item will be contained in our Definitive Proxy Statement under the heading "Independent Registered Public Accountants' Fees," and is incorporated herein by reference.

PART IV

Item 15. Exhibits, Financial Statement Schedules.

(a) Documents filed as a part of this Report:

(1) Financial Statements.

The financial statements of Crinetics Pharmaceuticals, Inc., together with the reports thereon of BDO USA, P.C., an independent registered public accounting firm, are included in this Annual Report on Form 10-K.

(2) Financial Statement Schedules.

All schedules are omitted because they are not applicable, or the required information is shown in the financial statements or notes thereto.

(3) Exhibits.

A list of exhibits to this Annual Report on Form 10-K is set forth on the Exhibit Index immediately preceding the signature page and is incorporated herein by reference.

Item 16. Form 10-K Summary

None.

CRINETICS PHARMACEUTICALS, INC.
INDEX TO FINANCIAL STATEMENTS

Report of Independent Registered Public Accounting Firm

Stockholders and Board of Directors
Crinetics Pharmaceuticals, Inc.
San Diego, California

Opinion on the Consolidated Financial Statements

We have audited the accompanying consolidated balance sheets of Crinetics Pharmaceuticals, Inc. (the "Company") as of December 31, 2025 and 2024, the related consolidated statements of operations and comprehensive loss, stockholders' equity, and cash flows for each of the three years in the period ended December 31, 2025, and the related notes (collectively referred to as the "consolidated financial statements"). In our opinion, the consolidated financial statements present fairly, in all material respects, the financial position of the Company at December 31, 2025 and 2024, and the results of its operations and its cash flows for each of the three years in the period ended December 31, 2025**,** in conformity with accounting principles generally accepted in the United States of America.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States) ("PCAOB"), the Company's internal control over financial reporting as of December 31, 2025, based on criteria established in *Internal Control – Integrated Framework (2013)* issued by the Committee of Sponsoring Organizations of the Treadway Commission ("COSO") and our report dated February 26, 2026 expressed an unqualified opinion thereon.

Basis for Opinion

These consolidated financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on the Company's consolidated financial statements based on our audits. We are a public accounting firm registered with the PCAOB and are required to be independent with respect to the Company in accordance with the U.S. federal securities laws and the applicable rules and regulations of the Securities and Exchange Commission and the PCAOB.

We conducted our audits in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the consolidated financial statements are free of material misstatement, whether due to error or fraud.

Our audits included performing procedures to assess the risks of material misstatement of the consolidated financial statements, whether due to error or fraud, and performing procedures that respond to those risks. Such procedures included examining, on a test basis, evidence regarding the amounts and disclosures in the consolidated financial statements. Our audits also included evaluating the accounting principles used and significant estimates made by management, as well as evaluating the overall presentation of the consolidated financial statements. We believe that our audits provide a reasonable basis for our opinion.

Critical Audit Matter

The critical audit matter communicated below is a matter arising from the current period audit of the consolidated financial statements that was communicated or required to be communicated to the audit committee and that: (1) relates to accounts or disclosures that are material to the consolidated financial statements and (2) involved our especially challenging, subjective, or complex judgments. The communication of a critical audit matter does not alter in any way our opinion on the consolidated financial statements, taken as a whole, and we are not, by communicating the critical audit matter below, providing a separate opinion on the critical audit matter or on the accounts or disclosures to which it relates.

Accrued Clinical Trial Costs

As described in Notes 2 and 5 to the consolidated financial statements, the expenses and accrual for clinical trial activities are determined based on management's estimates of when services are provided by contract research organizations ("CROs") and other third parties. Estimates are determined by reviewing cost information provided by CROs, other third-party vendors, and internal clinical personnel, and the scope of work to be performed from contractual arrangements with CROs. As of December 31, 2025, the Company recorded $7.4 million in accrued clinical trial costs, which was included in accounts payable and accrued expenses on the consolidated balance sheets.

We identified the estimation of accrued clinical trial costs as a critical audit matter. Management's judgment was required to estimate the progress of services and the associated costs incurred, which were used to determine the accrued liabilities for clinical trial expenses. Auditing accrued clinical trial costs was especially challenging due to the nature and extent of audit effort required to address the matter.

The primary procedures we performed to address this critical audit matter included:

- Testing management's process for estimating accrued clinical trial costs by: (i) obtaining and inspecting certain agreements and related amendments and (ii) confirming total clinical trial costs incurred and total amounts billed with certain third-party vendors.
- Testing the completeness of the Company's accrued clinical trial costs by: (i) evaluating internal materials and publicly available information (such as press releases and public databases that track clinical trials) and (ii) testing invoices received after year-end from certain third-party vendors.

/s/ BDO USA, P.C.

We have served as the Company's auditor since 2016.

San Diego, California

February 26, 2026

CRINETICS PHARMACEUTICALS, INC.

Consolidated Balance Sheets
(In thousands, except per share amounts)

	December 31, 2025	December 31, 2024
ASSETS		
CURRENT ASSETS		
Cash and cash equivalents	$ 101,536	$ 264,545
Restricted cash	—	500
Investment securities, amortized cost of $924,317 at December 31, 2025 and $1,088,561 at December 31, 2024	926,353	1,089,524
Trade accounts receivable, net	592	—
Inventory	2,022	—
Prepaid expenses and other current assets	17,839	20,819
Total current assets	1,048,342	1,375,388
Property and equipment, net	14,296	12,068
Operating lease right-of-use assets	40,492	43,507
Restricted cash, net of current portion	800	800
Prepaid expenses and other assets, net of current portion	22,327	2,829
TOTAL ASSETS	$ 1,126,257	$ 1,434,592
LIABILITIES AND STOCKHOLDERS' EQUITY		
CURRENT LIABILITIES		
Accounts payable and accrued expenses	$ 41,770	$ 21,469
Accrued compensation and related expenses	35,578	28,887
Deferred revenue	1,235	2,176
Operating lease liabilities	6,489	7,152
Total current liabilities	85,072	59,684
Operating lease liabilities, non-current	42,052	44,570
Deferred revenue, non-current	3,810	4,704
Other non-current liabilities	3,240	829
TOTAL LIABILITIES	134,174	109,787
Commitments and contingencies (Note 7)		
STOCKHOLDERS' EQUITY		
Preferred stock, $0.001 par; 10,000 shares authorized, no shares issued or outstanding at December 31, 2025 or 2024	—	—
Common stock and paid-in capital, $0.001 par; 200,000 shares authorized, 95,575 shares issued and outstanding at December 31, 2025; 92,926 shares issued and outstanding at December 31, 2024	2,407,757	2,275,952
Accumulated other comprehensive income	1,865	963
Accumulated deficit	(1,417,427)	(952,110)
Stock held in trust	(112)	—
TOTAL STOCKHOLDERS' EQUITY	992,083	1,324,805
TOTAL LIABILITIES AND STOCKHOLDERS' EQUITY	$ 1,126,257	$ 1,434,592

See the accompanying notes to these consolidated financial statements.

CRINETICS PHARMACEUTICALS, INC.

Consolidated Statements of Operations and Comprehensive Loss
(In thousands, except per share data)

	Year ended December 31,		
	2025	2024	2023
Revenue:			
Product revenue, net	$ 5,420	$ —	$ —
Collaboration and license revenue	2,276	1,039	4,013
Total revenue, net	7,696	1,039	4,013
Operating expenses:			
Cost of product revenue	1,076	—	—
Research and development	332,058	240,156	168,527
Selling, general and administrative	191,331	99,737	58,094
Total operating expenses	524,465	339,893	226,621
Loss from operations	(516,769)	(338,854)	(222,608)
Other income (expense):			
Interest income	51,989	41,435	13,436
Other expense, net	(357)	(519)	(159)
Total other income, net	51,632	40,916	13,277
Loss before income taxes	(465,137)	(297,938)	(209,331)
Income tax expense	180	—	—
Loss before equity method investment	(465,317)	(297,938)	(209,331)
Loss on equity method investment	—	(470)	(5,198)
Net loss	$ (465,317)	$ (298,408)	$ (214,529)
Net loss per share:			
Net loss per share - basic and diluted	$ (4.95)	$ (3.69)	$ (3.69)
Weighted average shares - basic and diluted	94,057	80,783	58,071
Other comprehensive income (loss):			
Unrealized gain (loss) on investment securities	$ 1,074	$ (14)	$ 4,908
Unrealized loss on foreign currency	(172)	—	—
Total other comprehensive income (loss)	902	(14)	4,908
Comprehensive loss	$ (464,415)	$ (298,422)	$ (209,621)

See the accompanying notes to these consolidated financial statements.

CRINETICS PHARMACEUTICALS, INC.

Consolidated Statements of Stockholders' Equity
(in thousands)

	Common Stock Shares	Common Stock and Paid-In Capital	Accumulated Other Comprehensive Income (Loss)	Accumulated Deficit	Stock Held in Trust	Total Stockholders' Equity
Balance at January 1, 2023	53,877	$ 759,432	$ (3,931)	$ (439,173)	$ —	$ 316,328
Issuance of common stock, net of transaction costs	12,787	369,080	—	—	—	369,080
Issuance of common stock upon vesting of restricted stock units	81	—	—	—	—	—
Exercise of stock options	1,283	20,091	—	—	—	20,091
Stock issued under Employee Stock Purchase Plan	147	2,291	—	—	—	2,291
Stock-based compensation	—	40,937	—	—	—	40,937
Comprehensive income	—	—	4,908	—	—	4,908
Net loss	—	—	—	(214,529)	—	(214,529)
Balance at December 31, 2023	68,175	1,191,831	977	(653,702)	—	539,106
Issuance of common stock, net of transaction costs	21,986	970,048	—	—	—	970,048
Issuance of common stock upon vesting of restricted stock units	249	—	—	—	—	—
Exercise of stock options	2,294	40,463	—	—	—	40,463
Stock issued under Employee Stock Purchase Plan	222	4,224	—	—	—	4,224
Stock-based compensation	—	69,386	—	—	—	69,386
Comprehensive loss	—	—	(14)	—	—	(14)
Net loss	—	—	—	(298,408)	—	(298,408)
Balance at December 31, 2024	92,926	2,275,952	963	(952,110)	—	1,324,805
Issuance of common stock upon vesting of restricted stock units	415	—	—	—	—	—
Exercise of stock options	2,028	35,402	—	—	—	35,402
Stock issued under Employee Stock Purchase Plan	206	5,219	—	—	—	5,219
Stock-based compensation	—	91,024	—	—	—	91,024
Stock held in trust under deferred compensation plan	—	112	—	—	(112)	—
Other	—	48	—	—	—	48
Comprehensive income	—	—	902	—	—	902
Net loss	—	—	—	(465,317)	—	(465,317)
Balance at December 31, 2025	95,575	$ 2,407,757	$ 1,865	$ (1,417,427)	$ (112)	$ 992,083

See the accompanying notes to these consolidated financial statements.

CRINETICS PHARMACEUTICALS, INC.

Consolidated Statements of Cash Flows
(In thousands)

	Year ended December 31,		
	2025	**2024**	**2023**
CASH FLOWS FROM OPERATING ACTIVITIES			
Net loss	$ (465,317)	$ (298,408)	$ (214,529)
Reconciliation of net loss to net cash used in operating activities:			
Stock-based compensation	91,024	69,386	40,937
Depreciation and amortization	3,890	2,785	1,098
Noncash lease expense	3,014	3,042	1,210
Accretion of purchase discounts and amortization of premiums on investment securities, net	(15,425)	(14,931)	(6,271)
Noncash license revenue	—	—	(2,000)
Loss on equity method investment	—	470	5,198
Loss on disposal of property and equipment	50	51	6
Changes in operating assets and liabilities:			
Trade accounts receivable	(592)	—	—
Inventory	(2,022)	—	—
Prepaid expenses and other assets	(16,511)	(5,974)	(4,523)
Accounts payable and accrued expenses, compensation and related expenses, and other non-current liabilities	28,983	13,317	12,357
Deferred revenue	(1,835)	74	(1,535)
Operating lease liabilities	(3,181)	(6)	(546)
Net cash used in operating activities	(377,922)	(230,194)	(168,598)
CASH FLOWS FROM INVESTING ACTIVITIES			
Purchases of investment securities	(1,004,427)	(1,146,772)	(527,857)
Purchase of Radionetics preferred stock	—	—	(5,000)
Maturities and sale of investment securities	1,184,097	575,799	337,132
Purchases of property and equipment	(5,762)	(3,844)	(4,688)
Net cash provided by (used in) investing activities	173,908	(574,817)	(200,413)
CASH FLOWS FROM FINANCING ACTIVITIES			
Proceeds from issuance of common stock, net of commissions	—	985,030	369,560
Offering costs related to issuance of common stock	—	(14,982)	(541)
Proceeds from exercise of stock options and shares issued under Employee Stock Purchase Plan	40,611	44,611	22,216
Net cash provided by financing activities	40,611	1,014,659	391,235
Net change in cash, cash equivalents and restricted cash	(163,403)	209,648	22,224
Exchange rate changes on cash, cash equivalents and restricted cash	(106)	—	—
Cash, cash equivalents and restricted cash - beginning of period	265,845	56,197	33,973
Cash, cash equivalents and restricted cash - end of period	$ 102,336	$ 265,845	$ 56,197
COMPONENTS OF CASH, CASH EQUIVALENTS AND RESTRICTED CASH:			
Cash and cash equivalents	$ 101,536	$ 264,545	$ 54,897
Restricted cash	800	1,300	1,300
Cash, cash equivalents and restricted cash at end of period	$ 102,336	$ 265,845	$ 56,197
NON-CASH INVESTING AND FINANCING ACTIVITIES			
Private company shares received under licensing arrangements	$ —	$ —	$ 2,000
Exercise of Radionetics Warrant	$ —	$ —	$ 668
Stock options exercised receivable	$ 10	$ 76	$ 166
Receivable for common stock issuances	$ —	$ —	$ 87
Accrued financing costs	$ —	$ —	$ 26
Stock held in trust	$ 112	$ —	$ —
Amounts accrued for purchases of property and equipment	$ 389	$ 180	$ 872
Right-of-use asset obtained in exchange for lease obligations	$ —	$ —	$ 46,273
Leasehold improvements paid by the lessor	$ —	$ —	$ 2,925

See the accompanying notes to these consolidated financial statements.

CRINETICS PHARMACEUTICALS

Notes to Consolidated Financial Statements
(Unless otherwise indicated, all amounts are presented in thousands, except per share amounts)

1. Organization and Basis of Presentation

Description of Business

Crinetics Pharmaceuticals Inc. (the "Company") is a pharmaceutical company committed to transforming the treatment of endocrine diseases and endocrine-related tumors through science rooted in patient needs. The Company is focused on discovering, developing, and commercializing novel therapies, with core expertise in targeting G protein coupled receptors with small molecules that have specifically tailored pharmacology and properties.

The Company's lead product, PALSONIFY™ (paltusotine), is the first once-daily, oral treatment approved by the U.S. Food and Drug Administration ("FDA") for the treatment of adults with acromegaly who had an inadequate response to surgery and/or for whom surgery is not an option. Paltusotine is also in clinical development for carcinoid syndrome associated with neuroendocrine tumors ("NETs"). Our pipeline of disclosed programs includes late-stage investigational candidate atumelnant, which is currently in development for congenital adrenal hyperplasia and ACTH-dependent Cushing's syndrome, and CRN09682, a nonpeptide drug conjugate candidate that is being developed to treat somatostatin receptor type 2 ("SST2") expressing NETs and other SST2 expressing solid tumors. Additional discovery programs address a variety of endocrine conditions such as NETs, Graves' disease (including Graves' hyperthyroidism and Graves' orbitopathy, or Thyroid Eye Disease), polycystic kidney disease, hyperparathyroidism, diabetes, obesity, and GPCR-targeted oncology indications.

Liquidity

From inception, the Company has devoted substantially all of its efforts to drug discovery and development, conducting preclinical studies and clinical trials, and building the infrastructure necessary for commercial operations. The Company has a limited operating history and the sales and income potential of the Company's business and market are unproven. While the Company has received FDA approval for its lead product, the Company may continue to incur substantial operating losses even as it generates revenue from PALSONIFY, and a successful transition to attaining profitable operations is dependent upon achieving a level of revenue adequate to support the Company's cost structure.

The Company has experienced net losses and negative cash flows from operating activities since its inception and has an accumulated deficit of $1.4 billion as of December 31, 2025. As of December 31, 2025, the Company had $1.0 billion in cash, cash equivalents and investment securities, which the Company believes is sufficient to meet its funding requirements for at least the next 12 months.

On January 8, 2026, the Company completed an underwritten public offering of 8,763,000 shares of its common stock for net proceeds of approximately $380.0 million, after underwriting discounts, commissions and other offering costs.

The Company's future long-term liquidity requirements will be substantial and will depend on many factors, including the Company's ability to effectively commercialize PALSONIFY and other product candidates. The Company expects to continue to incur net losses for the foreseeable future and may need to raise substantial additional capital to accomplish its business objectives over the next several years. The Company plans to continue to fund its losses from operations and capital funding needs through a combination of its existing capital resources, product sales, equity offerings, debt financings or other sources, including potential collaborations, licenses and other similar arrangements. If the Company is not able to secure adequate additional funding, the Company may be forced to make reductions in spending, extend payment terms with suppliers, liquidate assets where possible, or suspend or curtail planned programs. Any of these actions could materially harm the Company's business, results of operations and prospects. There can be no assurance as to the availability or terms upon which such financing and capital might be available in the future.

2. Summary of Significant Accounting Policies

Basis of Presentation and Principles of Consolidation

The consolidated financial statements include the Company's accounts and those of its wholly-owned subsidiaries, and have been prepared inconformity with U.S. generally accepted accounting principles ("GAAP"). All intercompany transactions have been eliminated.

Reclassifications

Certain prior period amounts within the consolidated statements of cash flows have been reclassified to conform to the current period presentation. These reclassifications had no effect on the net change in cash.

Use of Estimates

The preparation of the Company's consolidated financial statements in conformity with U.S. GAAP requires it to make estimates and assumptions that impact the reported amounts of assets, liabilities, revenue and expenses and the disclosure of contingent assets and liabilities in the Company's consolidated financial statements and accompanying notes. The most significant estimates in the Company's consolidated financial statements relate to accrual of research and development expenses, valuation of stock-based awards, fair values of financial instruments, inventory valuation, revenue recognition, and the assumptions underlying the determination of the estimated incremental borrowing rate for the determination of the Company's operating lease right-of-use assets.

Estimates are based on current facts, historical experiences and/or on forecasts, including information received from third parties and various other factors that the Company believes are reasonable under the circumstances, the results of which form the basis for making judgments about the carrying values of assets and liabilities and the recording of revenue and expenses that are not readily apparent from other sources. Actual results may differ materially and adversely from these estimates. Estimates are periodically reviewed in light of changes in circumstances, facts and experience. Actual results could differ from those estimates. To the extent there are material differences between the estimates and actual results, the Company's future results of operations will be affected.

Investment in Radionetics

In October 2021, the Company, together with other investors, announced the formation of Radionetics Oncology, Inc. ("Radionetics").

The Company first analyzes its investment in another entity to determine if the entity is a variable interest entity ("VIE") and if so, whether the Company is the primary beneficiary requiring consolidation. An entity is considered a VIE if (1) the entity does not have enough equity to finance its own activities without additional support, (2) the entity's at-risk equity holders lack the characteristics of a controlling financial interest, or (3) the entity is structured with non-substantive voting rights. VIEs are consolidated by the primary beneficiary, which is the entity that has both the power to direct the activities that most significantly impact the VIE's economic performance and the obligation to absorb losses or the right to receive benefits from the VIE that potentially could be significant to the VIE. Variable interests in a VIE can be contractual, ownership, or other financial interests. The Company re-assesses its investment upon reconsideration events to determine whether the Company is the primary beneficiary of the VIE, in which case the Company would consolidate the VIE.

When it is determined that the Company is not the primary beneficiary but has the ability to exercise significant influence over the VIE, the Company accounts for the unconsolidated investment under the equity method of accounting.

Fair Value Measurements

The accounting guidance defines fair value, establishes a consistent framework for measuring fair value and expands disclosure for each major asset and liability category measured at fair value on either a recurring or non-recurring basis. Fair value is defined as an exit price, representing the amount that would be received to sell an asset or paid to transfer a liability in an orderly transaction between market participants. As such, fair value is a market-based measurement that should be determined based on assumptions that market participants would use in pricing an asset or liability. As a basis for considering such assumptions, the accounting guidance establishes a three-tier fair value hierarchy, which prioritizes the inputs used in measuring fair value as follows:

- Level 1: Observable inputs such as quoted prices in active markets;
- Level 2: Inputs, other than the quoted prices in active markets, that are observable either directly or indirectly; and
- Level 3: Unobservable inputs in which there is little or no market data, which require the reporting entity to develop its own assumptions about risk and the assumptions market participants would use in pricing the asset or liability developed based on the best information available in the circumstances.

The carrying amounts of the Company's current financial assets, restricted cash and current financial liabilities are considered to be representative of their respective fair values because of the short-term nature of those instruments. The Company's policy is to recognize transfers between levels of the fair value hierarchy on the date of the event or change in circumstances that caused the transfer.

Cash, Cash Equivalents and Restricted Cash

Cash and cash equivalents include cash held in readily available checking and money market accounts, as well as short-term debt securities with maturities of three months or less when purchased. Restricted cash represents cash held as collateral for the Company's lease and is reported as an asset in the accompanying consolidated balance sheets. Cash is considered a Level 1 investment.

Investment Securities

The Company's investments in debt securities are classified as available-for-sale and carried at fair value. Unrealized gains and losses are recorded in accumulated other comprehensive loss in the accompanying consolidated balance sheets. Investments are classified as short-term based on contractual maturity or the Company's ability and intent to liquidate the investments within the next twelve months.

The Company elected to exclude accrued interest from both the fair value and amortized costs basis of available-for-sale when assessing credit losses and to write-off any uncollectible accrued interest receivable as a reversal of interest income. Accrued interest receivable is recorded in prepaid expenses and other current assets in the accompanying consolidated balance sheets.

Realized gains and losses are determined using the specific identification method and are included in other income (expense), net. Interest income is recognized when earned.

At each reporting date, the Company evaluates available-for-sale debt securities in an unrealized loss position to determine whether losses should be recognized in earnings. The Company first assesses whether it intends to sell, or is more likely than not required to sell, the security before recovery of its amortized cost. If so, the amortized cost is written down to fair value through net loss. For securities not meeting these criteria, the Company evaluates whether the decline in fair value is due to credit losses, considering factors such as severity of impairment, interest rate changes, credit ratings, and expected recovery. Credit-related unrealized losses are recorded as an allowance in interest income. No impairments or credit losses were recognized during the periods presented.

Trade Accounts Receivable and Allowance

Trade accounts receivable arise from the product sales and represent amounts due from customers, which include a specialty distributor and specialty pharmacies. Trade accounts receivable are recorded at the invoiced amount and are non-interest bearing. Trade accounts receivable are presented net of reserves for distribution service fees and chargebacks.

The Company evaluates the collectability of trade accounts receivable on a regular basis, by reviewing the financial condition and payment history of its customers, the age of customer accounts, and general economic factors or events expected to affect future collections. An allowance for credit losses is recorded when a receivable is deemed to be uncollectible. The Company recorded no allowance for credit losses as of December 31, 2025.

Inventories

Inventories consist of raw materials, work in process, and finished goods held for sale and are stated at the lower of cost or net realizable value. Cost is determined using the first-in, first-out ("FIFO") method. Inventory valuation reserves are established, as a reduction to the cost basis of the asset, for excess, obsolete, or unsaleable inventory, as appropriate. The Company capitalizes inventory costs related to products when future economic benefit is considered probable and the related costs are expected to be recoverable. If the criteria for capitalizing inventory are not met, such costs are expensed as research and development. As a result, inventory on hand at the time of regulatory approval may have a zero cost basis.

Concentrations of Credit Risk

Financial instruments that potentially subject the Company to significant concentrations of credit risk consist primarily of cash, cash equivalents, investment securities. The Company maintains deposits in federally insured financial institutions in excess of federally insured limits. The Company has not experienced any losses in such accounts and believes it is not exposed to significant risk on its cash balances due to the financial position of the depository institution in which those deposits are held. Additionally, the Company has established guidelines regarding approved investments and maturities of investments, which are designed to maintain safety and liquidity.

The Company, through a 3PL, distributes PALSONIFY in the U.S. to its customers, The Company is subject to credit risk related to its accounts receivable from product sales, which are due from the specialty distributor and specialty pharmacies. These customers distribute products to a broad range of downstream channels, and the Company has not experienced material credit losses to date.

Leases

The Company determines whether an arrangement contains a lease at contract inception. Operating lease right-of-use ("ROU") assets and operating lease liabilities are recognized at the commencement date based on the present value of lease payments over the expected lease term, which includes renewal or termination options the Company is reasonably certain to exercise. Short-term leases with an initial term of twelve months or less are not recorded on the balance sheets.

The lease term includes renewal options that the Company is reasonably assured to exercise. Lease liabilities are measured using the Company's incremental borrowing rate when the implicit rate is not readily determinable.

Lease expense is recognized on a straight-line basis over the lease term. Variable lease costs are expensed as incurred. The Company accounts for lease and non-lease components as a single lease component.

Lease modifications are evaluated to determine whether they represent a separate contract. Modifications that are not separate contracts result in remeasurement of the lease liability using updated terms and the Company's revised incremental borrowing rate, with a corresponding adjustment to the ROU asset.

Property and Equipment, Net

Property and equipment are stated at cost, net of accumulated depreciation, and depreciated on a straight-line basis over their estimated useful lives. Estimated useful lives are generally as follows:

- Lab equipment: three to five years;
- Office equipment: three to five years; and
- Computer equipment and software: three years.

Leasehold improvements are amortized over the shorter of the estimated useful life of the improvement or the remaining lease term. Repairs and maintenance costs are expensed as incurred, while expenditures that materially extend the useful lives of assets are capitalized.

Impairment of Long-Lived Assets

The Company reviews long-lived assets for impairment whenever events or changes in circumstances indicate that the carrying amount of an asset or asset group may not be recoverable. An impairment loss is recognized when the carrying amount of the asset group exceeds the sum of the undiscounted future cash flows expected to result from its use and eventual disposition. If an asset group is determined to be impaired, the impairment loss is measured as the excess of the carrying amount over its fair value.

Deferred Compensation Plan

The Company has a non-qualified deferred compensation plan that provides directors and certain employees the ability to defer receipt of current cash compensation and vested restricted stock units until a later date. The assets are held in the Rabbi Trust and participants have the option to invest their cash deferrals in a fixed income investment, a defined set of mutual funds, and, with respect to deferrals of restricted stock units, in Company common stock. The Company has made an accounting policy election to assess instruments held in the Rabbi Trust at the instrument level. The assets of the Rabbi Trust are subject to the claims of creditors in the event that the Company becomes insolvent.

The deferred compensation liability related to cash deferrals is included in other liabilities in the Company's consolidated balance sheets and the deferred compensation asset related to cash deferrals is included in prepaid expenses and other assets, net of current portion in the Company's consolidated balance sheets. Changes in this liability balance are recorded to expense and reflected within operating expenses of the Company's consolidated statements of operations and comprehensive loss. Changes in the fair value of these assets are recorded within other income (expense) in the consolidated statements of operations and comprehensive loss.

Investments in shares of the Company's common stock are included as stock held in trust, in the Company's consolidated balance sheets. The participant's deferred compensation liability attributable to the participants' investments in shares of the Company's common stock are included within common stock and paid-in capital in the Company's consolidated balance sheets.

Revenue Recognition

The Company's revenue consist of product sales of PALSONIFY and revenue derived from its collaborative and licensing arrangements. The Company recognizes revenue when, or as, the control of the promised goods or services are transferred to customers in an amount that reflects the consideration to which it expects to be entitled in exchange for those goods or services. To determine revenue recognition for arrangements, the Company performs the following five steps: (1) identify the contract(s) with a customer; (2) identify the performance obligation(s) in the contract; (3) determine the transaction price; (4) allocate the transaction price to the performance obligation(s) in the contract; and (5) recognize revenue when (or as) the performance obligation(s) are satisfied. At contract inception, the Company assesses the goods or services promised within each contract, assesses whether each promised good or service is distinct and identifies those that are performance obligations. The Company recognizes as revenue the amount of the transaction price that is allocated to the respective performance obligation when, or as, the performance obligation is satisfied. In revenue arrangements involving third parties, the Company recognizes revenue as the principal when it maintains control of the product or service until it is transferred to our customer; under other circumstances, the Company recognizes revenue as an agent in the sales transaction. Determining whether the Company has control requires judgment over certain considerations, which generally

include whether the Company is responsible for the fulfillment of the underlying products or services, whether it has inventory risk before fulfillment is completed, and if it has discretion to establish prices over the products or services. The Company evaluates whether it is the principal or the agent in revenue arrangements involving third parties should there be changes impacting control in transferring related goods or services to customers.

Product Sales

The Company, through a 3PL, distributes PALSONIFY in the U.S. to its customers, who then sell the product to other end-user customers. The Company maintains control throughout the sales transactions as the principal and recognizes revenue when control of the product transfers, generally upon delivery, to its customers in an amount that reflects the consideration received or expected to be received. Payment terms with customers are within approximately two months from invoice date.

The Company sells PALSONIFY at Wholesale Acquisition Cost ("WAC") and calculates product revenue net of variable consideration and consideration payable to third parties associated with distribution of product. The Company utilizes the expected value method when estimating the amount of variable consideration to include in the transaction price. Variable consideration is included in the transaction price only to the extent it is probable that a significant revenue reversal will not occur. These amounts include government rebates, chargebacks, distribution service fees, co-payment assistance and return reserve, which are collectively referred to as “Gross-to-Net Adjustments.” Because all product sales commissions relate to contracts with a benefit period of less than one year, the Company expenses these commissions as incurred. Commissions are recorded in selling, general and administrative expenses in the consolidated statements of operations.

The Company must make significant judgments to determine the estimate for certain Gross-to-Net Adjustments. The specific considerations that the Company uses in estimating the amounts related to Gross-to-Net Adjustments are as follows:

Government Rebates

Government rebates represent estimated obligations to government agencies under the Medicaid Drug Rebate Program, Medicare Part D program. Government rebates represent estimated obligations to government agencies and are recorded based on the Company's best estimates, which consider a variety of factors, including payer mix and discount terms. These estimated rebates are recorded as accrued liabilities at the time the related product revenue is recognized.

Chargebacks

Chargebacks relate to the Company's estimated obligations resulting from contractual commitments to sell products to qualified entities at prices lower than the list prices that the Company charges. The Company estimates the chargebacks that it expects to be obligated to provide based upon the terms of the applicable arrangements and the forecasted business mix. These estimated chargebacks are recorded as contra trade accounts receivable at the time the related product revenue is recognized.

Distribution Service Fees

The Company pays distribution service fees to its customers for services related to the distribution of PALSONIFY. These fees are contractually fixed as a percentage of WAC and are calculated at the time of sale based on the quantity of product purchased. The Company records these fees as contra trade accounts receivable at the time the related product revenue is recognized.

Copay Assistance

The Company offers co-payment assistance programs to commercially insured patients whose insurance plans require a co-payment at the time a prescription is filled. The Company estimates the cost of co-payment assistance based on estimated utilization, contractual program terms, and other relevant factors, including forecasted business mix. Co-payment programs estimates are included in accounts payable and accrued expenses on the consolidated balance sheets.

Return Reserve

The Company permits the return of product within a specified number of months prior to and after its expiration date, as well as returns resulting from incorrect shipments or damaged or defective product, which the Company expects to be rare. The Company estimates expected product returns based on current experience and expectations. Expected product returns are accounted for as variable consideration and recorded as a reduction of product revenue in the period the related sales are recognized. A refund liability for expected returns is included in accrued expenses on the consolidated balance sheets. The Company will adjust its estimates in future periods if actual experience or expectations change.

Collaborative and Licensing Arrangements

The Company has entered into licensing and collaboration agreements that mainly include the following: (i) upfront considerations; (ii) payments associated with achieving certain milestones; and (iii) royalties based on specified percentages of net product sales, if any.

At the inception of an arrangement, the Company evaluates whether the arrangement falls within ASC 808, *Collaborative Arrangement*s, and/or ASC 606, *Revenue from Contracts with Customers*, and identifies the distinct performance obligations. Judgment is applied in determining whether the Company acts as principal or agent, whether licenses are functional or symbolic, and whether obligations are satisfied over time or at a point in time.

Milestone payments that are within the Company's control are included in the transaction price when it is probable that significant revenue reversal will not occur. Milestones outside the Company's control, such as regulatory approvals, are recognized when achieved. Sales-based royalties and milestone payments related to sales are recognized when the related sale occurs or the associated performance obligation is satisfied.

Transaction prices are allocated to performance obligations based on their estimated standalone selling prices. For obligations satisfied over time, the Company generally uses an input method, such as cost-to-cost, to measure progress, updating estimates each reporting period as necessary. Significant judgments include estimating costs, probabilities of success, development timelines, and other assumptions used to determine standalone selling prices and progress towards completion.

Cost of Product Revenue

Cost of product revenue consists of the purchase costs for finished products from third-party manufacturers, freight and handling from the Company's 3PL logistics service provider, and certain salary-related and stock-based compensation expenses for employees involved in manufacturing, quality control, and supply chain activities.

Manufacturing costs incurred for inventory produced prior to regulatory approval, for which there is no alternative future use, are expensed as research and development in the period incurred. As a result, inventory manufactured prior to regulatory approval that is subsequently approved and sold has a zero cost basis and does not result in cost of product revenue upon sale.

Cost of product revenue also reflects any write-downs or reserve adjustments for the Company's inventories and commercial manufacturing readiness and supplier qualification costs incurred for approved products, where activities relate to commercialization rather than research and development.

Research and Development Expenses

Research and development ("R&D") expenses consist of personnel-related costs, including salaries, benefits, payroll taxes, and stock-based compensation for employees engaged in R&D activities, as well as costs for third-party research and development services, laboratory supplies, clinical materials, and allocated facilities and depreciation costs. R&D expenses are expensed as incurred.

Costs incurred under contracts with contract research organizations ("CROs") and other third parties that conduct and manage the Company's clinical trials are included in R&D expenses and are accrued based on estimates of services performed to date. Estimates are determined by reviewing cost information provided by CROs, other third-party vendors, and internal clinical personnel, and the scope of work to be performed from contractual arrangements with CROs. Payments made in advance of the receipt of goods or services to be used in R&D activities are recorded as prepaid expenses and expensed as the related goods or services are received.

Advertising Expenses

Advertising costs are expensed as incurred and are included in selling, general and administrative expenses. Advertising costs for the year ended December 31, 2025 were approximately $16.9 million. Advertising costs for the years ended December 31, 2024 and 2023 were not significant to the Company's consolidated financial statements.

Stock-Based Compensation

Stock-based compensation expense represents the estimated grant date fair value of the Company's equity awards, consisting of stock options, restricted stock units and shares issued under the Company's Employee Stock Purchase Plan ("ESPP"), recognized over the requisite service period of such awards (usually the vesting period) on a straight-line basis and recognizes forfeitures as they occur. The Company estimates the fair value of all stock option grants and the ESPP using the Black-Scholes option pricing model.

The key assumptions used in determining the fair value of stock options grants and ESPP, and the Company's rationale, were as follows:

(i) *Expected term* - the expected term for stock options represents the period that the stock options are expected to be outstanding and has been estimated using the simplified method, due to limited historical exercise behavior. The expected term using the simplified method is an average of the contractual option term and its vesting period; the expected term for awards granted under the ESPP represents the term the awards are expected to be outstanding;

(ii) *Expected volatility* - the expected volatility assumption for stock-based awards granted is based on the historical volatility of the Company's common stock;

(iii) *Risk-free interest rate* - the risk-free interest rate is based on the U.S. Treasury yield in effect at the time of grant for zero coupon U.S. Treasury notes with maturities that approximate the expected terms of awards; and

(iv) *Expected dividend yield* - the expected dividend yield assumption is zero as the Company has never paid dividends and has no present intention to do so in the future.

Restricted stock units are valued using the closing sale price of the Company's common stock on the date of grant.

Income Taxes

The Company accounts for income taxes using the asset and liability method, under which deferred tax assets and liabilities are recognized for the expected future tax consequences of temporary differences between the financial statement carrying amounts and the tax bases of assets and liabilities. Deferred tax assets and liabilities are measured using enacted tax rates expected to apply in the periods in which the temporary differences are expected to reverse.

Deferred tax assets are reduced by a valuation allowance when, based on the weight of available evidence, it is more likely than not that some portion or all of the deferred tax assets will not be realized.

The Company accounts for uncertain tax positions using a two-step approach under which tax positions are recognized when it is more likely than not that the position will be sustained upon examination, and measured as the largest amount of tax benefit that is more than 50% likely to be realized upon settlement. Interest and penalties related to uncertain tax positions are recognized within income tax expense.

Recently Adopted Accounting Pronouncements

ASU 2023-09

In December 2024, the Financial Accounting Standards Board ("FASB") issued Accounting Standards Update ("ASU") No. 2023-09, Income Taxes (Topic 740): *Improvements to Income Tax Disclosures* ("ASU 2023-09"). ASU 2023-09 requires disaggregated information about a reporting entity's effective tax rate reconciliation as well as information on income taxes paid. ASU 2023-09 is effective for public entities with annual periods beginning after December 15, 2024, with early adoption permitted. The Company adopted this standard in the current period retrospectively for all periods presented (see Note 12).

Recent Accounting Pronouncements Not Yet Adopted

ASU 2024-03

In November 2024, the FASB issued ASU 2024-03, *Income Statement–Reporting Comprehensive Income–Expense disaggregation Disclosures (Subtopic 220-40): Disaggregation of Income Statement Expenses* ("ASU 2024-03"), which requires disaggregated disclosure of income statement expenses for public business entities ("PBEs"). The ASU does not change the expense captions an entity presents on the face of the income statement; rather, it requires disaggregation of certain expense captions into specified categories in disclosures within the footnotes to the financial statements. ASU 2024-03 is effective for all PBEs for fiscal years beginning after December 15, 2026, and interim periods within fiscal years beginning after December 15, 2027. Early adoption is permitted. The Company is currently evaluating the impact that this guidance will have on the presentation of its consolidated financial statements and accompanying notes.

ASU 2025-03

In May 2025, the FASB issued ASU 2025-03, *Business Combinations (Topic 805) and Consolidation (Topic 810): Determining the Accounting Acquirer in the Acquisition of a Variable Interest Entity* ("ASU 2025-03"), which provides guidance for identifying the accounting acquirer in business combinations in which the legal acquiree is a VIE that meets the definition of a business. Under the ASU, the acquirer is determined using the factors in Accounting Standards Codification 805, Business Combinations ("ASC 805") rather than assuming the primary beneficiary is the acquirer. ASU 2025-03 is effective for fiscal years beginning after December 15, 2026, and interim periods within those years, with early

adoption permitted. The Company is currently evaluating the impact of this guidance on the presentation of its consolidated financial statements and accompanying notes.

3. Investment Securities

The Company reports its available-for-sale investment securities at their estimated fair values. The following is a summary of the available-for-sale investment securities held by the Company as of December 31, 2025 and 2024:

	As of December 31, 2025				As of December 31, 2024			
	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Fair Market Value	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Fair Market Value
Available-for-sale investment securities:								
Corporate debt securities	$ 510,668	$ 1,215	$ (11)	$ 511,872	$ 487,613	$ 818	$ (182)	$ 488,249
Agency obligations	43,997	1	(29)	43,969	57,986	2	(57)	57,931
U.S. government obligations	369,652	860	—	370,512	542,962	417	(35)	543,344
Total	$ 924,317	$ 2,076	$ (40)	$ 926,353	$ 1,088,561	$ 1,237	$ (274)	$ 1,089,524

As of December 31, 2025 and 2024, available-for-sale investment securities by contractual maturity were as follows:

	As of December 31, 2025		As of December 31, 2024	
	Amortized Cost	Fair Market Value	Amortized Cost	Fair Market Value
Available-for-sale investment securities:				
Due in one year or less	$ 712,675	$ 714,118	$ 621,499	$ 622,161
Due after one year through five years	211,642	212,235	467,062	467,363
Total	$ 924,317	$ 926,353	$ 1,088,561	$ 1,089,524

The following is a summary of the available-for-sale investment securities by length of time in a net loss position as of December 31, 2025 and 2024:

	As of December 31, 2025		As of December 31, 2024	
	Less Than 12 Months		Less Than 12 Months	
	Fair Market Value	Gross Unrealized Losses	Fair Market Value	Gross Unrealized Losses
Available-for-sale investment securities:				
Corporate debt securities	$ 38,596	$ (11)	$ 165,032	$ (182)
Agency obligations	27,471	(29)	47,936	(57)
U.S. government obligations	—	—	19,953	(35)
Total	$ 66,067	$ (40)	$ 232,921	$ (274)

As of December 31, 2025 and 2024, all available-for-sale investment securities in a continuous unrealized loss position had been in a loss position for less than 12 months.

The Company reviewed its investment holdings as of December 31, 2025 and 2024 and determined that the decrease in fair value is attributable to changes in interest rates and not credit quality, and as the Company does not intend to sell the investments and it is not more likely than not that the Company will be required to sell the investments before recovery of their amortized cost basis, which may be maturity. Therefore, there were no allowances for credit losses as of December 31, 2025 and 2024. During the years ended December 31, 2025, 2024, and 2023, the realized net gains (losses) recognized in the accompanying statements of operations and comprehensive loss were not significant.

Accrued interest receivable on available-for-sale securities was $7.8 million and $8.3 million at December 31, 2025 and 2024, respectively. The Company did not write off any accrued interest receivable in any of the periods presented in the consolidated financial statements.

4. Fair Value Measurements

Fair value measurements may be based on trade prices in active markets for identical assets or liabilities (Level 1 inputs) or valuation models using inputs that are observable either directly or indirectly (Level 2 inputs), such as quoted prices for similar assets or liabilities, yield curves, volatility factors, credit spreads, default rates, loss severity, current market and contractual prices for the underlying instruments or debt, and broker and dealer quotes, as well as other relevant economic measures.

Financial assets measured at fair value on a recurring basis as of December 31, 2025 and 2024 were as follows:

	As of December 31, 2025			
	Level 1	Level 2	Level 3	Total
Cash equivalents:				
Money market funds	$ 70,731	$ —	$ —	$ 70,731
Total cash equivalents	70,731	—	—	70,731
Investment securities:				
U.S. government obligations	370,512	—	—	370,512
Agency obligations	—	43,969	—	43,969
Corporate debt securities	—	511,872	—	511,872
Total investment securities	370,512	555,841	—	926,353
Other non-current assets:				
Deferred compensation plan (1)	3,249	—	—	3,249
Total assets measured at fair value	$ 444,492	$ 555,841	$ —	$ 1,000,333

	As of December 31, 2024			
	Level 1	Level 2	Level 3	Total
Cash equivalents:				
Money market funds	$ 249,116	$ —	$ —	$ 249,116
Corporate debt securities	—	5,314	—	5,314
Total cash equivalents	249,116	5,314	—	254,430
Investment securities:				
U.S. government obligations	543,344	—	—	543,344
Agency obligations	—	57,931	—	57,931
Corporate debt securities	—	488,249	—	488,249
Total investment securities	543,344	546,180	—	1,089,524
Other non-current assets:				
Deferred compensation plan (1)	829	—	—	829
Total assets measured at fair value	$ 793,289	$ 551,494	$ —	$ 1,344,783

(1) Consists of mutual fund investments held in the Rabbi Trust related to the Company's non-qualified deferred compensation plan.

There were no transfers into or out of Level 3 during the years ended December 31, 2025 and 2024.

5. Balance Sheet Details

Inventory consisted of the following:

	December 31, 2025	December 31, 2024
Raw materials	$ —	$ —
Work in process	2,004	—
Finished goods	18	—
	$ 2,022	$ —

Inventory balances as of December 31, 2025 reflect the capitalization of PALSONIFY manufacturing costs following the regulatory approval in September 2025. PALSONIFY inventory produced prior to approval was expensed as research and development.

There were no write-downs of inventory for the year ended December 31, 2025.

Prepaid expenses and other assets consisted of the following:

	December 31, 2025	December 31, 2024
Prepaid clinical costs	$ 19,547	$ 6,842
Interest receivable	7,758	8,310
Deferred compensation plan	3,249	829
Prepaid research and development costs	2,901	714
Loyal preferred stock (Note 8)	2,000	2,000
Prepaid subscriptions	1,255	2,561
Other	3,456	2,392
Total prepaid expenses and other assets	40,166	23,648
Less prepaid expenses and other current assets	(17,839)	(20,819)
Prepaid expenses and other assets, net of current portion	$ 22,327	$ 2,829

Property and equipment, net consisted of the following:

	December 31, 2025	December 31, 2024
Leasehold improvements	$ 10,003	$ 11,900
Lab equipment	9,960	5,693
Office equipment	2,225	2,147
Computers and software	60	60
Property and equipment at cost	22,248	19,800
Less accumulated depreciation and amortization	(7,952)	(7,732)
Total	$ 14,296	$ 12,068

Depreciation and amortization expense was $3.9 million, $2.8 million and $1.1 million for the years ended December 31, 2025, 2024 and 2023, respectively.

Accounts payable and accrued expenses consisted of the following:

	December 31, 2025	December 31, 2024
Accounts payable	$ 22,611	$ 5,853
Accrued clinical trial costs	7,369	3,076
Accrued research and development costs	4,506	6,067
Accrued outside services and professional fees	4,430	5,572
Other accrued expenses	2,854	901
Total	$ 41,770	$ 21,469

6. Operating Leases

The Company's lease obligations consist of an operating lease for its headquarters in San Diego, California, entered into in 2022 (the “2022 Lease”). The Company's prior operating lease for a facility in San Diego, California, entered into in 2018, expired in August 2025.

Under the terms of the 2022 Lease, the Company's expected future monthly minimum lease payments of $0.5 million, with six months of rent abatement in the first year, start on the earlier of (i) the date which is ten (10) months after substantial completion of demolition work, or (ii) the date of the substantial completion of improvements and first occupancy for business purposes, and the term expires on the date immediately preceding the one hundred thirty-seventh (137th) monthly anniversary of this lease payment start date. Lease payments are subject to annual 3% increases. The Company is also responsible for certain operating expenses and taxes during the term of the 2022 Lease. The 2022 Lease provides the Company with specified tenant improvement and landlord work allowances. The Company has (i) two options to extend the term of the 2022 Lease for an additional period of 5 years each, and (ii) a right of first offer on adjacent space to the new facility, subject to the terms and conditions of the 2022 Lease. The 2022 Lease commenced in 2023 when the building was ready and available for its intended use. As of the date of the recording of the 2022 Lease, the Company is not reasonably certain that these options will be exercised.

The Company’s estimated incremental fully collateralized borrowing rate of 8.6% was used in its present value calculation as the 2022 Lease does not have a stated rate and the implicit rate was not readily determinable. The rate was determined using a synthetic credit rating analysis.

Under the terms of the 2018 Lease and 2022 Lease, the Company provided the lessors with irrevocable letters of credit in the amounts of $0.5 million and $0.8 million, respectively, the latter of which is included in restricted cash and restricted cash, net of current portion in the accompanying consolidated balance sheets. The $0.5 million letter of credit related to the 2018 Lease, which was included in restricted cash in the accompanying consolidated balance sheet as of December 31, 2024, was released as of December 31, 2025. The lessor of the 2022 Lease is entitled to draw on the $0.8 million letter of credit in the event of any default by the Company under the terms of the lease.

As of December 31, 2025, the Company's future minimum payments under non-cancellable operating leases, were as follows:

Year ending December 31,	Minimum Payments
2026	$ 6,795
2027	6,999
2028	7,209
2029	7,425
2030	7,648
Thereafter	35,903
Total future minimum lease payments	71,979
Less imputed interest	(23,438)
Total operating lease liabilities	48,541
Less operating lease liabilities, current	(6,489)
Operating lease liabilities, non-current	$ 42,052

Operating lease cost was $8.4 million, $8.5 million, and $3.3 million for each of the years ended December 31, 2025, 2024 and 2023, respectively. Short-term lease expenses for the years ended December 31, 2025, 2024 and 2023 were not significant.

Remaining lease terms and discount rates for the Company's operating leases are as follows:

	As of December 31, 2025 (1)	As of December 31, 2024
Weighted-average remaining lease term (years)	9.3 years	10.1 years
Weighted-average discount rate	8.6%	8.6%

(1) Reflects only the Company's 2022 Lease as the 2018 Lease expired in August 2025.

Supplemental cash flow information related to leases was as follows:

	Year Ended December 31,		
	2025	2024	2023
Operating cash flow used for operating leases	$ 7,468	$ 4,491	$ 1,616

7. Commitments and Contingencies

Litigation

From time to time, the Company may be subject to various claims and suits arising in the ordinary course of business. The Company does not expect that the resolution of these matters will have a material adverse effect on its financial position or results of operations.

8. Revenue Recognition

Product Revenue

Following the regulatory approval in September 2025, the Company launched PALSONIFY and began recognizing product revenue in the United States from the sales to specialty distributors and specialty pharmacies.

The following table summarizes customers that represented 10% or greater of our consolidated gross product revenue for the year ended December 31, 2025:

	Year Ended December 31, 2025
Customer A	58 %
Customer B	42 %

Sanwa Kagaku Kenkyusho Co., Ltd

On February 25, 2022, the Company and Sanwa Kagaku Kenkyusho Co., Ltd. ("SKK"), entered into a license agreement (the “SKK License”) whereby the Company granted SKK an exclusive license to develop and commercialize paltusotine in Japan.

Under the SKK License, SKK has the right to receive data obtained by the Company through certain paltusotine studies. The Company assessed the SKK License and concluded that SKK is a customer within the agreement. SKK will assume all costs associated with clinical trials and regulatory applications associated with these processes in Japan. Further, the Company retains all rights to develop and commercialize the product outside Japan. The Company also granted SKK the right to purchase supply of paltusotine for clinical and commercial requirements at cost plus a pre-negotiated percentage which was a market rate and therefore not a material right.

In exchange, the Company received a $13.0 million nonrefundable, upfront payment and will be eligible to receive up to an additional $25.5 million in milestone payments related to the achievement of certain development, regulatory and commercial goals. In addition, upon market approval of paltusotine in Japan, the Company will be eligible to receive certain sales-based royalties.

Initially, the Company determined that the transaction price amounted to the upfront payment of $13.0 million. The Company determined that its performance obligations under the SKK License consist of the license and data exchange.

The control of the license was transferred to SKK at the inception of the contract and the Company does not have an ongoing performance obligation to support or maintain the licensed intellectual property. Revenue allocated to the data exchange obligation is recognized over time using the cost-to-cost measure as this method represents a faithful depiction of

progress toward certain ongoing paltusotine studies and related data transfer. Revenue is recognized on a gross basis as the Company is the principal. As there have been no sales of paltusotine in Japan to date, no sales-based milestones or royalties were recognized to date. Further, using the most-likely-method, the other developmental milestone payments are considered fully constrained.

During the year ended December 31, 2024, the Company achieved a $1.0 million milestone for the first indication of the development milestones. In 2024, the Company updated its estimated transaction price to $14.0 million and recorded a cumulative catch-up adjustment of $0.4 million.

Deferred revenue consisted of the following:

	Year Ended December 31,		
	2025	2024	2023
Balance at beginning of period	$ 6,880	$ 6,806	$ 8,341
Deferred revenue additions, excluding amounts recognized as revenue during the period	—	550	—
Revenue recognized	(1,835)	(476)	(1,535)
Balance at end of period	5,045	6,880	6,806
Less deferred revenue, current	(1,235)	(2,176)	(2,056)
Deferred revenue, non-current	$ 3,810	$ 4,704	$ 4,750

During the years ended December 31, 2025, 2024, and 2023, $1.8 million, $0.9 million, and $1.5 million, respectively, of the $14.0 million estimated transaction price was recognized as revenue in the accompanying consolidated statements of operations and comprehensive loss. Deferred revenue are expected to be recognized over the duration of certain paltusotine studies conducted by the Company.

On June 14, 2022, the Company and SKK, entered into a clinical supply agreement (the "SKK Clinical Supply Agreement") whereby the Company is responsible for manufacturing and supplying certain materials to SKK for specified activities under the SKK License. During the years ended December 31, 2025, 2024 and 2023, the Company recognized $0.4 million, $0.1 million, and $0.4 million respectively, of revenue from the SKK Clinical Supply Agreement in the accompanying consolidated statements of operations and comprehensive loss.

Cellular Longevity, Inc., doing business as Loyal

On March 24, 2023, the Company and Cellular Longevity Inc., doing business as Loyal ("Loyal") entered into a license agreement (the “Loyal License”) whereby the Company granted Loyal an exclusive license to develop and commercialize CRN01941, a somatostatin receptor type 2 agonist, for veterinary use. In exchange the Company received a $0.1 million nonrefundable, upfront payment and Loyal preferred stock valued at approximately $2.0 million. The Company may also earn single-digit sales-based royalties if the product is approved.

No revenue was recognized during the year ended December 31, 2025 and 2024. During the year ended December 31, 2023, the Company recognized $2.1 million of revenue from the Loyal License at the inception of the contract in the accompanying consolidated statements of operations and comprehensive loss. As of December 31, 2025, the shares of Loyal preferred stock issued and to be issued to the Company valued at $2.0 million is included in other assets in the accompanying consolidated balance sheets. The Loyal preferred stock does not have a readily determinable fair value and is recorded at cost less impairment.

9. Stockholders’ Equity

Stock Offerings

On March 1, 2024, the Company completed a private placement of 8,333,334 shares of its common stock at a price of $42.00 per share (the "Private Placement"). Net proceeds from the Private Placement were approximately $335.5 million, after offering costs of approximately $14.5 million. On March 19, 2024, the Company registered for resale the shares issued and sold in the Private Placement, pursuant to the Registration Rights Agreement entered into with the Purchasers, dated February 27, 2024.

On October 10, 2024, the Company completed an underwritten public offering of 11,500,000 shares of its common stock at a price to the public of $50.00 per share, which included 1,500,000 shares of common stock issued pursuant to the underwriters' option to purchase additional shares. Net proceeds from the offering were approximately $542.8 million, after underwriting discounts and commissions and other offering costs of approximately $32.2 million.

On January 8, 2026, the Company completed an underwritten public offering of 8,763,000 shares of its common stock at a price to the public of $45.95 per share, which included 1,143,000 shares of common stock issued pursuant to the underwriters' option to purchase additional shares. Net proceeds from the offering were approximately $380.0 million, after underwriting discounts and commissions and other offering costs.

ATM Offerings

On August 13, 2019, the Company entered into a Sales Agreement (as amended, the "2019 Sales Agreement") with SVB Leerink LLC and Cantor Fitzgerald & Co. (collectively, the "Sales Agents"), under which the Company could, from time to time, sell up to $150.0 million of shares of its common stock through the Sales Agents (the "2019 ATM Offering"). The 2019 ATM Offering was terminated upon the filing by the Company of its Registration Statement on Form S-3ASR on June 21, 2024.

On June 21, 2024, the Company entered into a Sales Agreement (the "2024 Sales Agreement") with the Sales Agents under which the Company may, from time to time, sell up to $350.0 million of shares of its common stock through the Sales Agents (the "2024 ATM Offering"). During the year ended December 31, 2025, and as of date of this Report, no shares of common stock have been issued pursuant to the 2024 ATM Offering. During the year ended December 31, 2024, the Company issued 1,223,775 shares of common stock for net proceeds of approximately $43.4 million and 928,912 shares of for net proceeds of approximately $48.3 million, pursuant to the 2019 ATM Offering and 2024 ATM Offering, respectively.

10. Equity Incentive Plans

2021 Employment Inducement Incentive Award Plan

The Company adopted the 2021 Employment Inducement Incentive Award Plan (the "2021 Inducement Plan") in December 2021. In December 2024, the Company amended the 2021 Inducement Plan to increase the number of shares of the Company's common stock available for future issuance under the 2021 Inducement Plan to 9,500,000 shares. The Company reserved 9,500,000 shares, as amended, of the Company's common stock for issuance pursuant to awards granted under the 2021 Inducement Plan. The terms of the 2021 Inducement Plan are substantially similar to the terms of the Company's 2018 Incentive Award Plan below with the exception that awards may only be made to an employee who has not previously been an employee or member of the board of directors of the Company if the award is in connection with commencement of employment. As of December 31, 2025, 1,982,536 shares of common stock were available for future issuance under the 2021 Inducement Plan.

2018 Incentive Award Plan

The Company adopted the 2018 Incentive Award Plan (the "2018 Plan") in July 2018. Under the 2018 Plan, which expires in July 2028, the Company may grant equity-based awards to individuals who are employees, officers, directors or consultants of the Company. Options issued under the 2018 Plan will generally expire ten years from the date of grant and vest over a four-year period. As of December 31, 2025, 5,494,874 shares of common stock were available for future issuance under the 2018 Plan.

The 2018 Plan contains a provision that allows annual increases in the number of shares available for issuance on the first day of each calendar year through January 1, 2028 in an amount equal to the lesser of: (i) 5% of the aggregate number of shares of the Company's common stock outstanding on December 31 of the immediately preceding calendar year, or (ii) such lesser amount determined by the Company. Under this evergreen provision, on January 1, 2026, an additional 4,778,774 shares became available for future issuance under the 2018 Plan.

2015 Stock Incentive Plan

The Company adopted the 2015 Stock Incentive Plan (the "2015 Plan") in February 2015, which provided for the issuance of equity awards to the Company's employees, members of its board of directors and consultants. In general, options issued under this plan vest over four years and expire after 10 years. Subsequent to the adoption of the 2018 Plan, no additional equity awards can be made under the 2015 Plan. The 2015 Plan expired in February 2025.

2018 Employee Stock Purchase Plan

The Company adopted the 2018 Employee Stock Purchase Plan (the "ESPP") in July 2018. The ESPP, which expires in July 2028, permits participants to purchase common stock through payroll deductions of up to 20% of their eligible compensation. As of December 31, 2025, 2,773,650 shares of common stock were available for issuance under the ESPP.

The ESPP contains a provision that allows annual increases in the number of shares available for issuance on the first day of each calendar year through January 1, 2028 in an amount equal to the lesser of: (i) 1% of the aggregate number of shares of the Company's common stock outstanding on December 31 of the immediately preceding calendar year, or (ii) such

lesser amount determined by the Company. The Company elected to not increase the number of shares available for issuance under the ESPP on January 1, 2026.

Stock Awards

Stock Options

Activity under the Company's stock option plans during the year ended December 31, 2025 was as follows:

	Options Outstanding	Weighted-Average Exercise Price	Weighted-Average Remaining Term (in years)	Aggregate Intrinsic Value (000's)
Balance on December 31, 2024	13,665,771	$ 26.57		
Granted	3,038,153	$ 35.85		
Exercised	(2,027,378)	$ 17.46		
Forfeited and expired	(1,045,472)	$ 33.27		
Balance on December 31, 2025	13,631,074	$ 29.54	7.2	$ 237,015
Exercisable on December 31, 2025	7,695,416	$ 25.28	6.3	$ 165,272

Aggregate intrinsic value is calculated as the difference at a specific point in time between the closing price of the Company's common stock at December 31, 2025 and the exercise price of stock options that had exercise prices below the closing price. The aggregate intrinsic value of options exercised during 2025, 2024 and 2023 was $46.5 million, $72.1 million and $16.2 million, respectively.

Restricted Stock Units

The Company's restricted stock unit activity during the year ended December 31, 2025 was as follows:

	Restricted Stock Units Outstanding	Weighted-Average Grant Date Fair Value
Balance on December 31, 2024	1,334,635	$ 34.30
Granted	1,624,023	$ 35.43
Vested	(415,264)	$ 32.51
Forfeited	(221,662)	$ 36.19
Balance on December 31, 2025	2,321,732	$ 35.23

The weighted average grant date fair value for restricted stock units granted during 2024 and 2023 was $43.56 and $19.62, respectively. The total fair value of restricted stock units that vested during 2025, 2024, and 2023 was $14.3 million and $10.0 million, and $1.4 million respectively.

Employee Stock Purchase Plan

During the year ended December 31, 2025, the Company issued 206,428 shares of our common stock under the ESPP. The shares were purchased by employees at an average purchase price of $25.28 per share, resulting in proceeds to the Company of approximately $5.2 million.

Fair Value of Stock Awards

The following table summarizes the weighted average assumptions used to estimate the fair value of stock options granted under the Company's stock option plans for the periods presented below:

Stock Option Awards	Year ended December 31,		
	2025	2024	2023
Expected option term	6.0 years	6.0 years	6.0 years
Expected volatility	64%	66%	66%
Risk free interest rate	4.3%	4.2%	4.1%
Expected dividend yield	—%	—%	—%

The weighted-average fair value of stock options awarded during the years ended December 31, 2025, 2024 and 2023 was $22.26, $28.96 and $13.09 per share, respectively.

The following table summarizes the weighted average assumptions used to estimate the fair value of the ESPP awards for the periods presented below:

ESPP	Year ended December 31,		
	2025	2024	2023
Expected term	1.3 years	1.3 years	1.1 years
Expected volatility	57%	72%	66%
Risk free interest rate	3.8%	5.0%	5.0%
Expected dividend yield	—%	—%	—%

The weighted-average fair value of awards under the ESPP during the years ended December 31, 2025, 2024 and 2023 was $13.40, $22.09 and $11.49 per share, respectively.

Restricted stock units are valued using the closing sale price of our common stock on the date of grant and recognizes forfeitures as they occur.

Stock-Based Compensation Expense

Stock-based compensation expense for the equity awards issued by the Company to employees and non-employees for the periods presented below was as follows:

	Year ended December 31,		
	2025	2024	2023
Included in research and development	$ 50,344	$ 40,667	$ 22,633
Included in general and administrative	40,680	28,719	18,304
Total stock-based compensation expense	$ 91,024	$ 69,386	$ 40,937

Total stock-based compensation expense capitalized during 2025 was not significant and not separately broken out above.

A summary of the Company's total unrecognized stock-based compensation expense, as of December 31, 2025, is as follows:

	Unrecognized Stock-Based Compensation Expense (in thousands)	Average Remaining Vesting Period (in years)
Stock option awards	$ 122,413	2.4
RSU awards	$ 61,297	2.7
ESPP	$ 6,600	1.4

11. Investment In Radionetics

Investment in Radionetics

In October 2021, the Company licensed its radiotherapeutics technology to Radionetics in exchange for 50,500,000 shares of Radionetics common stock, equivalent to a 64% initial stake, and a warrant to maintain up to 22% equity in Radionetics on a fully diluted basis (the “Radionetics Warrant”).

In August 2023, the Company participated in a refinancing transaction, exercising the Radionetics Warrant to purchase 3,407,285 shares of Radionetics common stock, exchanging 32,344,371 shares of Radionetics common stock for Radionetics preferred stock, and investing $5.0 million for an additional 14,404,656 shares of Radionetics preferred stock. The Radionetics license was also amended to include up to $15 million in new sales milestones.

In June 2024, the license with Radionetics was amended to reduce development targets, reverting certain rights to the Company, and the Company is eligible to receive total potential sales milestones in excess of $300.0 million and single-digit royalties on net sales. In July 2024, Radionetics formed a strategic partnership with Eli Lilly and Company (“Lilly”), receiving a $140.0 million upfront payment and granting Lilly the exclusive right to acquire Radionetics for $1.0 billion.

Although Radionetics is a VIE, the Company determined it is not the primary beneficiary and does not consolidate Radionetics' results due to lack of control over key decisions, which rest with Radionetics' independent board and management.

As of December 31, 2025, the Company owned approximately 25% of Radionetics consisting of common and preferred stock. The investment asset was previously written down to zero. Accordingly, during the year ended December 31, 2025, the Company recorded no equity method losses in the accompanying consolidated statements of operations and comprehensive loss, as a result of the allocation of the Company's share of Radionetics eligible losses, which is recorded on a quarterly lag.

Other Items

R. Scott Struthers, Ph.D., the Company's President and Chief Executive Officer, serves as chairman of the Radionetics board of directors. Pursuant to such arrangement, Dr. Struthers receives consideration in the form of both equity and a $50,000 annual retainer for his service as a board member of Radionetics. As of December 31, 2025, Dr. Struthers has an approximately 1.3% ownership stake in Radionetics consisting of common stock.

As of December 31, 2025 and 2024, the Company had no amounts due from Radionetics for reimbursement of certain expenses paid on behalf of Radionetics. Accordingly, no reimbursements were received by the Company during the year ended December 31, 2025. During the years ended December 31, 2024 and 2023, reimbursements from Radionetics were immaterial.

12. Income Taxes

For the three years in the period ended December 31, 2025, domestic and foreign pre-tax loss were:

	Year ended December 31,		
	2025	2024	2023
Loss before income taxes - Domestic	$ (453,630)	$ (297,441)	$ (208,829)
Loss before income taxes - Foreign	(11,507)	(497)	(502)
Loss before income taxes - Consolidated	$ (465,137)	$ (297,938)	$ (209,331)

The components of income tax expense are as follows in the period ended December 31, 2025:

	Year ended December 31,		
	2025	2024	2023
Current expense:			
U.S. Federal	$ —	$ —	$ —
State	—	—	—
Foreign	180	—	—
Total current expense (benefit)	180	—	—
Deferred expense:	—	—	—
U.S. Federal	—	—	—
State	—	—	—
Foreign	—	—	—
Total deferred expense (benefit)	—	—	—
Total expense (benefit)	$ 180	$ —	$ —

A reconciliation of income tax expense to the amount computed by applying the statutory federal income tax rate to the loss from operations for the three years in the period ended December 31, 2025 is as follows:

	Year ended December 31,					
	2025		2024		2023	
Tax computed at federal statutory rate	$ (97,679)	21.00 %	$ (62,666)	21.00 %	$ (45,051)	21.00 %
State tax, net of federal income tax effect (1)	(884)	0.19 %	(593)	0.20 %	(375)	0.17 %
Foreign tax effects	2,595	(0.56)%	104	(0.03)%	105	(0.05)%
Non-taxable or nondeductible items						
Stock-based compensation	104	(0.02)%	(7,395)	2.47 %	1,252	(0.58)%
Other	4,208	(0.90)%	2,487	(0.84)%	167	(0.08)%
Changes in valuation allowance	108,651	(23.36)%	84,071	(28.17)%	56,780	(26.47)%
Tax credits						
Federal R&D credits (2)	(20,550)	4.42 %	(19,527)	6.54 %	(15,455)	7.20 %
Other tax credits	(240)	0.05 %	—	— %	—	— %
Changes in unrecognized tax benefits	3,966	(0.85)%	3,515	(1.18)%	2,691	(1.25)%
Other adjustments						
Other	9	(0.01)%	4	0.01 %	(114)	0.06 %
Provision for income taxes	$ 180	(0.04)%	$ —	— %	$ —	— %

(1) The states that contribute to the majority (greater than 50%) of the tax effect in this category include California for 2025, 2024, and 2023.

(2) Federal R&D credits include research and development and orphan drug credits.

A summary of income taxes paid, net of refunds received, for the year ended December 31, 2025, 2024, and 2023 are as follows:

	Year ended December 31,		
	2025	2024	2023
Foreign			
Australia	89	—	—
Income taxes paid, net	$ 89	$ —	$ —

Deferred tax assets and liabilities

Net deferred tax assets are comprised of the following as of December 31, 2025 and 2024:

	December 31,	
	2025	2024
Deferred tax assets:		
Net operating loss carryforwards	$ 201,110	$ 109,135
Capitalized research expenses	71,799	83,785
R&D and other tax credits	79,999	57,901
Stock-based compensation	23,420	18,090
Lease liabilities	10,490	11,592
Accrued expenses and other, net	11,035	7,488
Equity method investment	3,418	3,544
Total deferred tax assets	401,271	291,535
Less: valuation allowance	(392,031)	(281,784)
Total deferred tax assets after valuation allowance	9,240	9,751
Deferred tax liabilities:		
Right-of use assets	(8,750)	(9,751)
Other deferred tax liabilities	(490)	—
Total deferred tax liabilities	(9,240)	(9,751)
Net deferred tax assets	$ —	$ —

Realization of deferred tax assets is dependent upon future earnings, if any, the timing and amount of which are uncertain. Management assesses the available positive and negative evidence to estimate if sufficient future taxable income will be generated to use existing deferred tax assets. Based on the weight of available evidence, including the Company's history of operating losses, management has determined that it is more likely than not that the Company's net deferred tax assets will not be realized. Accordingly, a valuation allowance has been established by the Company to fully offset these net deferred tax assets.

The Company is subject to taxation in the U.S., various state jurisdictions, Australia, Switzerland, Germany, Netherlands and Brazil; however, as it has operated at a loss since inception, it has not paid income taxes in any of the jurisdictions in which it has operated, except Australian withholding taxes. At December 31, 2025, the Company had federal, state, and foreign net operating loss ("NOL") carryforwards of approximately $861.8 million, $258.1 million and $14.2 million, respectively. The federal loss carryforwards generated after 2017 of $855.4 million will carry forward indefinitely and can be used to offset up to 80% of future annual taxable income, while those loss carryforwards generated prior to 2018 begin expiring in 2035, unless previously utilized. $5.1 million of the state loss carryforwards will carry forward indefinitely. The other state loss carryforwards begin expiring in 2035, unless previously utilized. Of the Company's foreign loss carryforwards, $10.1 million begin expiring in 2032, unless previously utilized, and the remaining loss carryforwards do not expire. The Company also has federal and California R&D credit carryforwards and federal Orphan Drug Credits totaling $42.4 million, $21.5 million, and $34.5 million, respectively. The federal R&D credits begin to expire in 2030, unless previously utilized, while the state credits do not expire. The federal Orphan Drug credit carryforwards will begin to expire in 2040, unless previously utilized.

The Company's NOL and credit carryforwards to offset future taxable income may be subject to a substantial annual limitation upon future utilization as a result of ownership changes that could occur in the future pursuant to Internal Revenue Code Sections 382 and 383. These ownership changes may limit the amount of NOL and credit carryforwards that can be utilized to offset future taxable income and tax, respectively. In general, an 'ownership change' as defined by the tax code results from a transaction or series of transactions over a three-year period resulting in an ownership change of more than 50 percent of the outstanding stock of a company by certain stockholders or public groups. During 2020, the Company completed a study to assess whether an ownership change within the meaning of Section 382 had occurred for the time period prior to July 15, 2020. The study identified several such ownership changes during the study period, which resulted in limitations on the annual utilization of the Company's NOL and credit carryforwards, or the "Tax Attribute" carryforwards; however, the study findings also indicated that none of the Company's Tax Attribute carryforwards generated during the study period would expire solely as a result of annual limitations on the utilization of such Tax

Attribute carryforwards. The Company updated the study for 2022 through 2025 and did not identify any additional ownership changes. Future ownership changes could still occur which might place further limits on the Company's ability to utilize its Tax Attribute carryforwards.

The Company's federal income tax returns from 2023 forward, state income tax returns from 2022 forward, and its Australian tax returns beginning in 2022 are subject to examination by tax authorities; however, the Company's tax attribute carryforwards such as NOLs and R&D credits generated in closed years remain subject to adjustment by the taxing authorities until the future tax years in which those attributes are utilized are closed to statute. No such audits are underway.

Changes to the Company's unrecognized tax benefits are summarized in the following table:

	Year ended December 31,		
	2025	2024	2023
Beginning balance	$ 10,689	$ 6,946	$ 4,110
Increase (decrease) for prior year tax positions	(20)	(85)	188
Increase (decrease) for current year tax positions	4,083	3,828	2,648
Decreases due to settlements	—	—	—
Expiration of the statute of limitations for the assessment of taxes	—	—	—
Ending balance	$ 14,752	$ 10,689	$ 6,946

Due to the existence of the valuation allowance, future changes in unrecognized tax benefits would not have any effect on the Company's effective tax rate. There have been no decreases in unrecognized tax benefits due to settlements or expiration of statute of limitations for the assessment of taxes during the years ended December 31, 2025, 2024 and 2023.

The Company's policy is to recognize the interest expense and/or penalties related to income tax matters as a component of income tax expense. The Company had no accrual for interest or penalties on its consolidated balance sheets as of December 31, 2025 or December 31, 2024, and has not recognized interest and/or penalties in its consolidated statements of operations for the years ended December 31, 2025, 2024, and 2023 as the unrecognized tax benefits relate to tax positions for which no cash tax liability has been reduced.

Deferred income taxes have not been provided for undistributed earnings of the Company's consolidated foreign subsidiaries because the Parent entity would not be required to include the distribution into income as the amount would be tax free. The Company has no foreign withholding tax liability as of December 31, 2025 as a result of losses in foreign subsidiaries.

The Tax Cuts and Jobs Act subjects a U.S. shareholder to tax on Global Intangible Low-Taxed Income ("GILTI") earned by certain foreign subsidiaries. The FASB Staff Q&A, Topic 740 No. 5. Accounting for Global Intangible Low-Taxed Income, states that an entity can make an accounting policy election to either recognize deferred taxes for temporary basis differences expected to reverse as GILTI in future years or to provide for the tax expense related to GILTI in the year the tax is incurred as a period expense only. We have elected to account for GILTI in the year the tax is incurred.

13. Segment Reporting

The Company identifies operating segments based on components of the business for which discrete financial information is available and that are regularly reviewed by the Chief Operating Decision Maker ("CODM") in allocating resources, assessing performance and monitoring budget versus actuals. The Company's CODM is its founder and Chief Executive Officer.

The Company operates as a single operating and reportable segment, focused on the discovery, development, and commercialization of therapeutics for rare endocrine diseases and endocrine-related tumors.

The segment derives revenue from product sales and licensing arrangements. The CODM evaluates performance using consolidated net loss, as presented in the consolidated statements of operations and comprehensive loss. Segment assets are represented by total consolidated assets reported in the consolidated balance sheets. Segment depreciation expense and capital expenditures are consistent with the consolidated amounts reported in the consolidated statements of cash flows due to the Company's single-segment structure.

Substantially all of the Company's assets and revenues are generated in the United States. The segment amount of equity method investments is also consistent with the consolidated amount reported in the consolidated balance sheets.

Segment revenue and significant segment expenses which are regularly reported to the CODM are included within the table below and are reconciled to consolidated net loss:

	Year ended December 31,		
	2025	2024	2023
Revenue:			
Product revenue, net	$ 5,420	$ —	$ —
Collaboration and license revenue	2,276	1,039	4,013
Total revenue, net	7,696	1,039	4,013
Less:			
Cost of product revenue	(1,076)	—	—
Research and development expenses			
Paltusotine	(68,337)	(51,229)	(46,772)
Atumelnant	(48,131)	(24,524)	(13,118)
Other research and development programs	(33,322)	(26,010)	(20,421)
Research and development personnel expenses	(102,677)	(70,772)	(53,446)
Research and development stock-based compensation	(50,344)	(40,667)	(22,633)
Other research and development (1)	(29,247)	(26,954)	(12,137)
Total research and development expenses	(332,058)	(240,156)	(168,527)
Selling, general and administrative			
External selling, general and administrative expenses	(90,013)	(38,733)	(20,362)
Selling, general and administrative personnel expenses	(60,638)	(32,285)	(19,428)
Selling, general and administrative stock-based compensation	(40,680)	(28,719)	(18,304)
Total selling, general and administrative expenses	(191,331)	(99,737)	(58,094)
Total other income, net	51,632	40,916	13,277
Income tax expense	(180)	—	—
Loss on equity method investment	—	(470)	(5,198)
Segment and consolidated net loss	$ (465,317)	$ (298,408)	$ (214,529)

(1) Other research and development is comprised of non-personnel related research and development indirect costs incurred for the benefit of multiple research and development programs, including depreciation, and other facility-based expenses, such as rent expense.

14. Net Loss Per Share

Basic net loss per share is computed by dividing the net loss by the weighted-average number of common shares outstanding for the period, without consideration for potentially dilutive securities. Diluted net loss per share is computed by dividing the net loss by the weighted-average number of shares of common stock and dilutive common stock equivalents outstanding for the period determined using the treasury-stock and if-converted methods. Dilutive common stock equivalents are comprised of common stock subject to repurchase and stock options outstanding under the Company's stock option plan. For all periods presented, there is no difference in the number of shares used to calculate basic and diluted shares outstanding as inclusion of the potentially dilutive securities on loss per share would be antidilutive.

Potentially dilutive securities (in common stock equivalent shares) not included in the calculation of diluted net loss per share because to do so would be anti-dilutive are as follows:

	Year ended December 31,		
	2025	2024	2023
Stock option awards	13,631	13,666	12,627
Unvested RSU awards	2,322	1,335	814
Estimated shares of common stock to be purchased under the ESPP	652	197	302
Stock held in trust under deferred compensation plan	3	—	—
Total	16,608	15,198	13,743

15. Defined Contribution Plan

The Company maintains a defined contribution 401(k) plan for eligible employees. The Company had accrued matching contribution liabilities of approximately $2.5 million, $1.0 million, and $0.7 million as of December 31, 2025, 2024 and 2023, respectively, which are included in accrued compensation and related expenses.

EXHIBIT INDEX

Exhibit Number	Exhibit Description	Incorporated by Reference			Filed Herewith
		Form	Date	Number	
3.1	Amended and Restated Certificate of Incorporation	8-K	7/20/2018	3.1	
3.2	Amended and Restated Bylaws	8-K	12/12/2023	3.1	
4.1	Specimen Stock Certificate Evidencing the Shares of Common Stock	S-1/A	7/09/2018	4.1	
4.2	Description of Registered Securities	10-K	3/30/2021	4.3	
10.1#	Crinetics Pharmaceuticals, Inc. 2015 Stock Incentive Plan, as amended	S-1/A	7/09/2018	10.1	
10.2#	Form of stock option agreement under Crinetics Pharmaceuticals, Inc. 2015 Stock Incentive Plan, as amended	S-1	6/22/2018	10.2	
10.3#	Crinetics Pharmaceuticals, Inc. 2018 Incentive Award Plan	S-1/A	7/09/2018	10.3	
10.4#	Form of stock option agreement under Crinetics Pharmaceuticals, Inc. 2018 Incentive Award Plan	S-1/A	7/09/2018	10.4	
10.5#	Form of restricted stock unit agreement under Crinetics Pharmaceuticals, Inc. 2018 Incentive Award Plan	10-K	3/30/2022	10.5	
10.6#	Crinetics Pharmaceuticals, Inc. 2018 Employee Stock Purchase Plan and offering document thereunder	S-1/A	7/09/2018	10.5	
10.7#	Amended and Restated Employment Agreement, effective as of May 25, 2018, by and between R. Scott Struthers and the Registrant	S-1	6/22/2018	10.6	
10.8#	Employment Agreement, effective as of June 15, 2018, by and between Alan Krasner, M.D. and the Registrant	S-1/A	7/09/2018	10.8	
10.9#	Form of Indemnification Agreement for Directors and Officers	S-1/A	7/09/2018	10.9	
10.10†	Lease Agreement, dated as of September 9, 2022, by and between San Diego 1 LLC and the Registrant	10-Q	11/14/2022	10.1	
10.11	First Amendment to Lease, dated December 8, 2023, to the Lease Agreement, dated as of September 9, 2022, by and between San Diego 1 LLC and the Registrant	10-K	2/28/2024	10.14	
10.12#	Crinetics Pharmaceuticals, Inc. 2021 Employment Inducement Incentive Award Plan and Form of Stock Option Agreement thereunder	8-K	12/23/2021	10.1	
10.13#	Amendment to the Crinetics Pharmaceuticals, Inc. 2021 Employment Inducement Incentive Award Plan	10-Q	11/14/2022	10.3	
10.14#	Amendment No. 2 to the Crinetics Pharmaceuticals, Inc. 2021 Employment Inducement Incentive Award Plan	10-K	2/28/2023	10.19	
10.15#	Amendment No. 3 to the Crinetics Pharmaceuticals, Inc. 2021 Employment Inducement Incentive Award Plan	10-Q	11/7/2023	10.1	
10.16#	Amendment No. 4 to the Crinetics Pharmaceuticals, Inc. 2021 Employment Inducement Incentive Award Plan	10-K	2/27/2025	10.19	

10.18#	Form of restricted stock unit agreement under Crinetics Pharmaceuticals, Inc. 2021 Employment Inducement Incentive Award Plan	10-K	3/30/2022	10.17	
10.19#	Crinetics Pharmaceuticals, Inc. Excess Deferral Plan Adoption Agreement	10-Q	5/9/2024	10.1	
10.20#	Amended and Restated Employment Agreement, effective as of May 22, 2018, by and between Stephen Betz and the Registrant	10-K	3/30/2022	10.18	
10.21#	Employment Agreement, effective as of September 13, 2021, by and between Jeff Knight and the Registrant	10-K	3/30/2022	10.19	
10.22#	Consulting Agreement, effective as of April 1, 2025, between Crinetics Pharmaceuticals, Inc. and Marc Wilson	8-K	04/04/2025	10.1	
10.23†#	Employment Agreement, effective as of February 21, 2025, between Crinetics Pharmaceuticals, Inc. and Tobin Schilke	10-Q	05/08/2025	10.2	
10.24#	Transition and Separation Agreement, dated as of December 16, 2025, between Crinetics Pharmaceuticals, Inc. and Dana Pizzuti	8-K	12/17/2025	10.2	
10.25#	Advisor Agreement, dated December 16, 2025, between Crinetics Pharmaceuticals, Inc. and Dana Pizzuti	8-K	12/17/2025	10.2	
10.26#	Employment Agreement, effective December 16, 2024, by and between Isabel Kalofonos and the Registrant	10-K	2/27/2025	10.27	
10.27#	Sales Agreement, dated June 21, 2024, by and among Crinetics Pharmaceuticals, Inc., Leerink Partners LLC and Cantor Fitzgerald & Co.	8-K	6/21/2024	1.1	
10.28#	Registration Rights Agreement, dated February 27, 2024, by and among Crinetics Pharmaceuticals, Inc. and the persons party thereto.	8-K	3/1/2024	10.2	
10.29†	License Agreement, dated as of February 25, 2022, by and between Sanwa Kagaku Kenkyusho Co., Ltd. and the Registrant	10-Q	5/12/2022	10.2	
19	Insider Trading Compliance Policy				X
23.1	Consent of BDO USA, P.C., independent registered public accounting firm				X
31.1	Certification of Principal Executive Officer Pursuant to Rules 13a-14(a) and 15d-14(a) under the Securities Exchange Act of 1934, as Adopted Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002				X
31.2	Certification of Principal Financial Officer Pursuant to Rules 13a-14(a) and 15d-14(a) under the Securities Exchange Act of 1934, as Adopted Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002				X
32.1*	Certification of Principal Executive Officer Pursuant to 18 U.S.C. Section 1350, as Adopted Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002				X
32.2*	Certification of Principal Financial Officer Pursuant to 18 U.S.C. Section 1350, as Adopted Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002				X
97#	Clawback Policy	10-K	2/28/2024	97	

101.INS	INLINE XBRL Instance Document – the instance document does not appear in the Interactive Data File because its XBRL tags	X
101.SCH	INLINE XBRL Taxonomy Extension Schema Document	X
101.CAL	INLINE XBRL Taxonomy Extension Calculation Linkbase Document	X
101.DEF	INLINE XBRL Taxonomy Extension Definition Linkbase Document	X
101.LAB	INLINE XBRL Taxonomy Extension Label Linkbase Document	X
101.PRE	INLINE XBRL Taxonomy Extension Presentation Linkbase Document	X
104	Cover Page Interactive Data File (embedded within the Inline XBRL document)	X

† Portions of this exhibit have been omitted in compliance with Regulation S-K Item 601(b)(10)(iv).
# Indicates management contract or compensatory plan.
* These certifications are being furnished solely to accompany this annual report pursuant to 18 U.S.C. Section 1350 and are not being filed for purposes of Section 18 of the Securities Exchange Act of 1934 and are not to be incorporated by reference into any filing of the Registrant, whether made before or after the date hereof, regardless of any general incorporation language in such filing.

SIGNATURES

Pursuant to the requirements of Section 13 or 15(d) of the Securities Exchange Act of 1934, as amended, the Registrant has duly caused this Report to be signed on its behalf by the undersigned, thereunto duly authorized**.**

Crinetics Pharmaceuticals, Inc.

Date: February 26, 2026

By: /s/ R. Scott Struthers, Ph.D.

R. Scott Struthers, Ph.D.
President and Chief Executive Officer

Pursuant to the requirements of the Securities Exchange Act of 1934, as amended, this Report has been signed below by the following persons on behalf of the Registrant in the capacities and on the dates indicated.

Name	Title	Date
/s/ R. Scott Struthers, Ph.D. **R. Scott Struthers, Ph.D.**	President, Chief Executive Officer and Director (principal executive officer)	February 26, 2026
/s/ Tobin Schilke **Tobin Schilke**	Chief Financial Officer (principal financial and accounting officer)	February 26, 2026
/s/ Wendell Wierenga, Ph.D. **Wendell Wierenga, Ph.D.**	Chairman of the Board of Directors	February 26, 2026
/s/ Camille Bedrosian, M.D. **Camille Bedrosian, M.D.**	Director	February 26, 2026
/s/ Caren Deardorf **Caren Deardorf**	Director	February 26, 2026
/s/ Matthew K. Fust **Matthew K. Fust**	Director	February 26, 2026
/s/ Weston Nichols, Ph.D. **Weston Nichols, Ph.D.**	Director	February 26, 2026
/s/ Stephanie Okey **Stephanie Okey**	Director	February 26, 2026
/s/ Rogério Vivaldi Coelho, M.D. **Rogério Vivaldi Coelho, M.D.**	Director	February 26, 2026

1. PURPOSE

Federal and state laws prohibit trading in the securities of a company while in possession of Material Nonpublic Information ("MNPI") and in breach of a duty of trust or confidence. These laws also prohibit anyone who is aware of MNPI from providing this information to others who may trade. Violating such laws can undermine investor trust, harm the reputation and integrity of Crinetics Pharmaceuticals, Inc. (together with any of its subsidiaries, the "Company"), and result in dismissal from the Company or even serious criminal and civil charges against the individual and the Company. The Company reserves the right to take whatever disciplinary or other measure(s) it determines in its sole discretion to be appropriate in any particular situation, including disclosure of wrongdoing to government authorities.

The purpose of the Insider Trading Policy (the "Policy") is to promote compliance with federal and state securities laws and to prevent illegal insider trading by all Company personnel. The Policy serves to protect the reputation and integrity of the Company and all individuals associated with it.

2. SCOPE

This Policy applies to all employees and officers of the Company and to all members of the Company's Board of Directors and their respective family members as well as agents acting on behalf of Company, including consultants and contractors of the Company ("Covered Persons").

Covered Persons are responsible for ensuring that immediate family members and members of their household comply with this Policy. This Policy also applies to any entities controlled by Covered Persons, including any corporations, limited liability companies, partnerships or trusts, and transactions by these entities should be treated for the purposes of this Policy as if they were for the individual's own account.

Notwithstanding the foregoing, this Policy, including without limitation, the preclearance requirements, blackout periods and prohibited transactions, does not apply to venture capital entities or other institutional investors, and the related transactions in the Company's securities by such entities, that may be affiliated with a director of the Company or for Company securities that a director may be deemed to have beneficial ownership of by virtue of such affiliation; provided, however, it is the responsibility of each such entity, in consultation with its own counsel (as appropriate), to determine compliance with applicable securities laws in considering whether to adhere to this Policy.

Questions regarding the Policy should be directed to the CFO, CLO or Compliance Officer, who are responsible for the administration of this Policy.

3. DEFINITIONS

TERM	DEFINITION
Blackout Period	A specific timeframe during which directors, executives, and certain employees are prohibited from buying or selling Company securities. The primary purpose is to prevent insider trading, which is the illegal use of material non-public information (MNPI) for financial gain.
Material Nonpublic Information (MNPI)	Information is considered "material" if there is a substantial likelihood that a reasonable investor would consider it important in deciding to buy, sell, or hold a Security, or if the information is likely to have a significant effect on the market price of the Security. Information can be positive or negative.

Pre-Clearance Person	Directors, Officers, Executives and other employees who are routinely aware of highly confidential information. This includes reports to the Office of the CEO and members of the Company's Disclosure Committee, e.g., GPLs, Corporate Strategy and Investor Relations.
Purchase	Defined broadly under the federal securities law and includes not only the actual purchase of a security, but also any contract to purchase or otherwise acquire a Security.
Purchase or Sell Securities	Extends to a broad range of transactions, including conventional cash-for-stock transactions, conversions, the exercise of stock options, transfers, gifts, and acquisitions and exercises of warrants or puts, calls, pledging and margin and, or other derivative Securities.
Quarterly Insiders	All executive officers; directors; individuals involved in the preparation of the Company's financial statements and/or the Company's periodic reports containing financial statements; all individuals who have information about the commercial performance of the Company or national level sales data; and any other individuals identified by the CFO, CLO or their designee.
Sale	Defined broadly under the federal securities law and includes not only the actual sale of a Security, but also any contract to sell or otherwise dispose of a Security.
Securities	Includes stocks, bonds, notes, debentures, options, warrants, equity and other convertible securities, as well as derivative instruments.

4. ABBREVIATIONS

ABBREVIATION	DEFINITION
BOD	Board of Directors
CEO	Chief Executive Officer
CFO	Chief Financial Officer
CLO	Chief Legal Officer
FDA	Food and Drug Administration
MNPI	Material Nonpublic Information
SEC	Securities and Exchange Commission

5. POLICY STATEMENTS

NO COVERED PERSON SHALL PURCHASE OR SELL ANY TYPE OF SECURITY WHILE IN POSSESSION OF MNPI RELATED TO THE SECURITY OR THE ISSUER OF SUCH SECURITY IN BREACH OF A DUTY OF TRUST OR CONFIDENCE, WHETHER THE ISSUER OF SUCH SECURITY IS THE COMPANY OR ANY OTHER COMPANY.

- Every Covered Person has ethical and legal obligations to maintain the confidentiality of information about the Company and to not engage in transactions in Company Securities while in possession of MNPI. A detailed discussion of MNPI can be found in section 5.3.
    - Covered Persons shall not directly or indirectly communicate MNPI to anyone outside the Company (except in accordance with the Company's policies regarding confidential information) or to anyone within the Company other than on a "need-to-know" basis.
- Additionally, if a Covered Person is in possession of MNPI about other publicly traded companies, such as suppliers, customers, competitors or potential acquisition targets, the Covered Person may

not trade in such other companies' securities until the information becomes public or is no longer material.

5.1 **Blackout Periods**

All Covered Persons are prohibited from trading in the Company's securities during Blackout Periods, as described below.

The purpose of the most frequent Blackout Period is to prevent anyone who is involved in the preparation of the Company's quarterly financial statements from trading before the Company's financial results are released and disseminated into the market. This Quarterly Blackout Period begins around the time that the appropriate personnel begin work on the company's financial statements and before the financial books and records for the period are closed. In our case, we have determined that fifteen (15) days before the end of the fiscal quarter is a reasonable standard start for the Quarterly Blackout Period, though in some instances, the CFO, CLO or their designee will determine and announce an earlier start for the Quarterly Blackout Period.

In addition to the Quarterly Blackout Period, periodically, the Company will impose Special Blackout Periods during which certain or all Covered Persons will be prohibited from buying, selling or otherwise effecting transactions Crinetics' securities.

In both instances, the Blackout Period only ends after the Company's financial results or other MNPI are publicly disclosed, allowing some extra time for the public to react to the information, (e.g., at the close of business on the first or second full trading day after the information is released.) However, it is critical to note that even if there is not a Company imposed Blackout Period, a Covered Person who is in possession of any MNPI should not trade in the Company's securities until the information has been made publicly available or is no longer material. Additional information about these two types of Blackout Periods is available below.

- **Quarterly Blackout Periods.** All executive officers; directors; individuals involved in the preparation of the Company's financial statements and/or the Company's periodic reports containing financial statements[1]; all individuals who have information about the commercial performance of the Company or national level sales data; and any other individuals identified by the CFO, CLO or their designee (collectively "**Quarterly Insiders**") are prohibited from trading in the Company's securities during the period beginning two weeks before the end of each fiscal quarter and ending at the close of business on the second trading day following the date the Company's financial results are publicly disclosed through the applicable SEC filing. During these periods, Quarterly Insiders generally possess or are presumed to possess material nonpublic information about the Company's financial results and performance.
- **Special Blackout Periods.** Periodically, the Company may also place restrictions on Covered Persons who possess or are likely to possess MNPI about major corporate announcements. To

[1] Such individuals include the following:
- Finance employees.
- Investor Relations and Corporate Communications Department employees that assist with preparing earnings releases.
- Legal department employees that prepare (or assist with preparing) a company's Form 10-K and Form 10-Q reports.
- Company officers, executive leadership and employees that serve as members of the disclosure committee.
- Individuals with access to sales and commercial data and results.

avoid even the appearance of trading on inside information, those Covered Persons may not trade in the Company's securities during these additional Blackout Periods. Such Special Blackout Periods may occur, for example, when the Company releases revenue forecasts, announces clinical study results, engages in any significant business transaction, or investigates and assesses cybersecurity incidents.

- **Exceptions: Quarterly Blackout Periods and Special Blackout Periods do not apply to:**

    - Purchases of the Company's Securities from the Company pursuant to the Employee Stock Purchase Plan, or sales of the Company's Securities to the Company;
    - Exercises of stock options or other equity awards or the surrender of shares to the Company in payment of the exercise price or in satisfaction of any tax withholding obligations in a manner permitted by the applicable equity award agreement, or vesting of equity-based awards, in each case, that do not involve a Sale of the Company's Securities (the "cashless exercise" of a Company stock option or other equity award through a broker does involve a market sale of the Company's Securities, and therefore would not quality under this exception); or
    - Purchases or sales of the Company's Securities
        Mandated under an employee benefit plan maintained by the Company which authorizes the sale of only such securities as are necessary to satisfy tax withholding obligations arising exclusively from the vesting of a compensatory award, or
        Made pursuant to a plan adopted to comply with the Exchange Act Rule 10b5-1 (Rule 10b5-1).
    - Exceptions to the Blackout Period policy may be approved by the CFO and the CLO including any exceptions for bona fide gifts of the Company's Securities.

5.2 **Pre-clearance of Transactions by Directors, Officers, Executives and Certain Employees (Schedule 1)**

- All transactions (including gifts) in the Company's Securities by directors, officers, executives and any Covered Person listed on Schedule I (as amended from time to time) (each, a "**Pre-Clearance Person**") must be precleared by the CFO, CLO, or their designee. Pre-clearance should not be understood to represent legal advice by the Company that a proposed transaction complies with the law.
- A request for pre-clearance must be made in writing, at least three (3) business days in advance of the proposed transaction, and should include the identity of the Pre-Clearance Person, a description of the proposed transaction, the proposed date of the transaction, and the number of shares or other Securities involved. In addition, the Pre-Clearance Person must execute a certification that they are not aware of MNPI about the Company. The CFO, CLO or their designee shall have sole discretion to decide whether to clear any contemplated transaction. All transactions that are precleared must be effected within five (5) business days of receipt of the preclearance. A pre-cleared transaction (or any portion of a pre-cleared transaction) that has not been effected during the five (5) business day period must be submitted for pre-clearance determination again prior to execution. Notwithstanding receipt of pre-clearance, if the Pre-Clearance Person becomes aware of MNPI or becomes subject to a Blackout Period before the transaction is effected, the transaction may not be completed. Transactions under a previously established Rule 10b5-1 Trading Plan that has been preapproved in accordance with this Policy are not subject to further pre-clearance.
- The pre-clearance form is included here for all request for pre-clearance: Pre-Clearance Request Form
- None of the Company, the CFO, CLO, or the Company's other employees will have any liability for any delay in reviewing, or refusal of, a request for pre-clearance.

5.3 **Material Nonpublic Information**

For purposes of this Policy, information is "material" if a reasonable investor would consider it important in making a decision to buy, hold, or sell securities. If the information would affect your decision whether to buy or sell, it likely would have the same effect on others.

MNPI is not limited to historical facts but also includes projections and forecasts, including, but not limited to:

- Corporate earnings or earnings forecasts
- National sales data, revenue, forecasts or commercial results
- Strategic plans or go to market decisions
- Clinical trial results
- Product and research developments
- Significant cybersecurity or privacy incidents
- Significant personnel changes
- Government inspections, approvals, or other regulatory actions
- Collaborations, mergers, or acquisitions
- Major litigation
- Significant borrowings or financings
- Stock splits
- Defaults on borrowings
- Bankruptcies
- Cancellation of a material contract with a major customer, vendor or distributor that could have a material impact on the Company's finances

MNPI does not have to be related solely to the Company. For example, advanced knowledge of the contents of a forthcoming news article expected to affect the market price of the Company's securities can be material. Additionally, the fact that the Company is evaluating a transaction with another company may constitute MNPI regarding the other company. Other examples of material information about another company include research and/or development agreements, in-licensing or out-licensing of products or product candidates, acquisitions or other business combinations, and strategic equity investments by the Company.

- Covered Persons should remember that the threshold for what is considered material may differ for other companies. When in doubt, err on the side of caution and consult the Legal or Compliance department before trading or disclosing information.
- Information is "nonpublic" if it is not available to the general public. For information to be considered "public" it must be widely disseminated in a manner that makes it generally available to investors in a Regulation FD-compliant method, such as through a press release, a filing with the US Securities and Exchange Commission (SEC) or a Regulation FD-compliant conference call.
- The CFO, CLO or their designee shall have sole discretion to decide whether information is public for purposes of this Policy.
- In all cases, the responsibility for determining whether an individual is in possession of MNPI rests with that individual. Any action on the part of the Company, the CFO or CLO, or any other employee or director pursuant to the Policy (or otherwise) does not in any way constitute legal advice or insulate an individual from liability under applicable securities laws.
- The circulation of rumors, even if accurate and reported in the media, does not constitute public dissemination. In addition, even after a public announcement, a reasonable period of time may need to lapse for the market to react to the information. Generally, the passage of one or two full trading days following release of the information to the public is a reasonable waiting period before such information is deemed public.

5.4 **Post-Termination Transactions**

This Policy continues to apply to transactions in Company securities even after termination of service to the Company. If an individual is in possession of MNPI when the individual's service terminates, the individual may not trade in the Company's securities until that information has become public or is no longer material.

5.5 **Prohibited Transactions**

In order to protect both Covered Persons and Crinetics, it is important to avoid the appearance as well as the fact of insider trading or disclosure of MNPI. Therefore, it is against this Policy for Covered Persons to directly or indirectly participate in transactions involving trading activities that by their nature are aggressive or speculative or may give rise to an appearance of impropriety. Covered Persons may not:

- Engage in short sales (sale of stock that the seller does not own or a sale that is completed by delivery of borrowed stock) with respect to Crinetics securities;
- Purchase or pledge Crinetics stock on margin or as collateral to secure a loan or other obligation (with the exception of the use of a margin account to purchase Crinetics common stock in connection with the exercise of Crinetics-granted stock options); or
- Enter into any derivative or similar transactions with respect to Crinetics securities. Examples of prohibited derivative transactions include, but are not limited to, purchases or sales of puts and calls (whether written or purchased or sold); options (whether "covered" or not); forward contracts, including but not limited to prepaid variable forward contracts; put and call "collars"; "equity" or "performance" swap or exchange agreements or any similar agreements or arrangements however denominated in Crinetics securities.
    - **Hedging**: Hedging transactions (e.g., prepaid variable forwards, equity swaps, collars, exchange funds) that offset or reduce the risk of ownership of Company Securities are prohibited.
    - **Margin and Pledging**: Covered Persons may not purchase Company Securities on margin, pledge them as collateral, or hold them in a margin account without prior written approval from the CFO.
    - **Standing or Limit Orders**: Standing or limit orders beyond one day are discouraged unless under an approved Rule 10b5-1 plan.

5.6 **Rule 10B5-1 Trading Plans**

Covered Persons, including Quarterly Insiders and Pre-Clearance Persons, may trade under a pre-approved Rule 10b5-1 Trading Plan that meets the following requirements:

- **Preapproval**: The plan must be submitted to and approved by the CFO or CLO, or their designee, before adoption or modification.
- **Cooling-Off Period**:
    - Section 16 officers: Later of 90 days after adoption or two (2) business days after filing the Form 10-Q/10-K for the quarter in which the plan was adopted (up to 120 days).
    - All others: 30 days after adoption.
- **Good Faith**: The plan must be adopted when the individual is not in possession of MNPI and outside any restricted period.
- **Plan Details**: The plan must specify trade amounts, prices, and dates, or include a written formula or algorithm, and prohibit the individual from influencing trades after adoption.
- **Duration**: Minimum six (6) months, maximum two (2) years.
- **Modifications**: Allowed only outside restricted periods, require preapproval, and may trigger a new cooling-off period.

- **One Plan Rule**: Only one (1) active plan at a time; only one single-trade plan per twelve (12) months (with limited exceptions).

The Company may impose additional conditions, require disclosures, and suspend or terminate plans if deemed necessary. Compliance with Rule 10b5-1 remains the individual's responsibility.

5.7 **Interpretation, Amendment, and Implementation of this Policy**

- The CFO, CLO and Compliance Officer shall have the authority to interpret and update this Policy and all related policies and procedures. In particular, such interpretations and updates of this Policy, as authorized by the CFO, CLO or Compliance Officer, may include amendments to or departures from the terms of this Policy (including amendments to Quarterly Insiders or the Pre-Clearance Persons identified in Schedule 1) to the extent consistent with the general purpose of this Policy and applicable securities laws.
- Actions taken by the Company, the CFO, CLO or any other Company personnel do not constitute legal advice, nor do they insulate you from the consequences of noncompliance with this Policy or with Securities laws.

6. REFERENCES

- CORP-POL-0004, Crinetics Code of Conduct and Ethics

7.

Schedule I

Individuals Subject to Pre-Clearance Requirement

Members of the Executive Leadership Team;

Members of the Company's Board of Directors; and

Members of the Disclosure Committee.

Exhibit 23.1

Consent of Independent Registered Public Accounting Firm

We hereby consent to the incorporation by reference in the Registration Statements on Form S-3 (Nos. 333-278060 and 333-280407) and Form S-8 (Nos. 333-226234, 333-254883, 333-264005, 333-268328, 333-270125, 333-275366, 333-277484 and 333-285342) of Crinetics Pharmaceuticals, Inc. (the Company) of our reports dated February 26, 2026, relating to the consolidated financial statements, and the effectiveness of the Company's internal control over financial reporting, which appear in this Annual Report on Form 10-K.

/s/ BDO USA, P.C.
San Diego, California

February 26, 2026

Exhibit 31.1

CERTIFICATION OF CHIEF EXECUTIVE OFFICER PURSUANT TO SECTION 302 OF THE SARBANES-OXLEY ACT OF 2002

I, R. Scott Struthers, Ph.D., certify that:

1. I have reviewed this annual report on Form 10-K of Crinetics Pharmaceuticals, Inc.;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer(s) and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

   (a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

   (b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

   (c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

   (d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, could significantly affect, or is reasonably likely to materially affect, the registrant's internal control over financial reporting, including any corrective actions with regard to any significant deficiencies and material weaknesses; and

5. The registrant's other certifying officer(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

   (a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

   (b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: February 26, 2026

/s/ R. Scott Struthers, Ph.D.

R. Scott Struthers, Ph.D.

President and Chief Executive Officer

Exhibit 31.2

CERTIFICATION OF CHIEF FINANCIAL OFFICER PURSUANT TO SECTION 302 OF THE SARBANES-OXLEY ACT OF 2002

I, Tobin Schilke, certify that:

1. I have reviewed this annual report on Form 10-K of Crinetics Pharmaceuticals, Inc.;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer(s) and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

   (a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

   (b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

   (c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

   (d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, could significantly affect, or is reasonably likely to materially affect, the registrant's internal control over financial reporting, including any corrective actions with regard to any significant deficiencies and material weaknesses; and

5. The registrant's other certifying officer(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

   (a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

   (b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: February 26, 2026

/s/ Tobin Schilke

Tobin Schilke

Chief Financial Officer

Exhibit 32.1

CERTIFICATION OF CHIEF EXECUTIVE OFFICER

Pursuant to 18 U.S.C. § 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, the undersigned officer of Crinetics Pharmaceuticals, Inc. (the "Company") hereby certifies, to his knowledge, that:

(i) the accompanying Annual Report on Form 10-K of the Company for the fiscal year ended December 31, 2025 (the "Report") fully complies with the requirements of Section 13(a) or Section 15(d), as applicable, of the Securities Exchange Act of 1934, as amended; and

(ii) the information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

/s/ R. Scott Struthers, Ph.D.

R. Scott Struthers, Ph.D.

President and Chief Executive Officer

Date: February 26, 2026

The foregoing certification is being furnished solely pursuant to 18 U.S.C. Section 1350 and is not being filed as part of the Report or as a separate disclosure document.

Exhibit 32.2

CERTIFICATION OF CHIEF FINANCIAL OFFICER

Pursuant to 18 U.S.C. § 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, the undersigned officer of Crinetics Pharmaceuticals, Inc. (the "Company") hereby certifies, to his knowledge, that:

(i) the accompanying Annual Report on Form 10-K of the Company for the fiscal year ended December 31, 2025 (the "Report") fully complies with the requirements of Section 13(a) or Section 15(d), as applicable, of the Securities Exchange Act of 1934, as amended; and

(ii) the information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

/s/ Tobin Schilke

Tobin Schilke

Chief Financial Officer

Date: February 26, 2026

The foregoing certification is being furnished solely pursuant to 18 U.S.C. Section 1350 and is not being filed as part of the Report or as a separate disclosure document.